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SHIFT WORK DISORDER: PREVALENCE, MANIFESTATION, AND RECOVERY

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DOCTORAL DISSERTATION

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ABSTRACT

Background: Approximately 20% of the workforce is exposed to shift work in Finland. A significant proportion of these workers experience insomnia and/or excessive sleepiness related to their shift work schedule, a phenomenon called shift work disorder (SWD). The International Classification of Sleep Disorders (ICSD) criteria for SWD were updated in the third edition (ICSD-3) in 2014, but scientific publications on SWD prevalence are still mainly based on the ICSD-2 criteria. Furthermore, SWD screening instruments vary significantly and are based on self-reports. Regardless of its prevalence among shift workers, little is known about the manifestation of SWD in real life. Similarly, it is not known whether those with SWD recover from their symptoms on days off. Accordingly, the aim of this thesis is to elucidate how the composition of work shifts and the SWD definitions applied associate with the SWD prevalence estimate, and how SWD manifests in relation to work shifts and free time.

Methods: This study includes two independent sets of data; 1) cross-sectional survey data from the ongoing longitudinal Working Hours in the Finnish Public Sector (WHFPS) cohort 2015 study, linked to registry data on working hours among hospital employees, and 2) questionnaires and three-week field data from an SWD study of ground staff at a Finnish airport.

Based on the objective working-hour data, 4 831 hospital employees were classified as shift workers without night shifts, shift workers with night shifts, or permanent night workers. To screen individuals for SWD on the basis of different criteria, the SWD survey responses were linked to working-hour registry data. SWD prevalence was estimated among groups with ≥ 1, ≥ 3, ≥ 5, and ≥ 7 non-day shifts (working hours outside 06:00–18:00 hours) per month. In addition, employees responded to questions about insomnia on weekly days off, excessive sleepiness on weekly days off, and their 24-hour sleep length.

The ground staff members were allocated to either the SWD (n = 22) or reference (n = 9) group by a questionnaire. Measurements included questionnaires and a three-week sleep diary and actigraphy monitoring. In addition, during the three-week field study, the participants assessed themselves using the Karolinska Sleepiness Scale (KSS), took Psychomotor Vigilance Tests (PVT), and carried out EEG-based sleep recordings on pre-selected morning shift days, night shift days, and days off.

Results: The ICSD-3-based SWD prevalence estimate varied between 3% and 4% among hospital shift workers without night shifts, between 3% and 10% among those with night shifts, and was 6% among permanent night workers, according to the cut-off of non-day shifts. The ICSD-2 criteria produced higher

SWD prevalence estimates: 7%–9%, 6%–34%, and 17%, respectively. SWD was more prevalent among shift workers with night shifts than among those without night shifts when cut-offs of ≥ 1–3 non-day shifts were applied.

Among the hospital employees, ICSD-2-based SWD was positively related to excessive sleepiness on days off and negatively related to insomnia on days off. In addition, SWD characterised by shift-related insomnia (but not excessive sleepiness) was positively related to excessive sleepiness on days off and to shorter 24-hour sleep length.

When using subjective field measures, the ground staff members with SWD had a shorter total sleep time and longer sleep debt prior to morning shifts than the reference group. Unlike the reference group, the SWD group appeared to have little compensatory sleep on days off. Furthermore, the SWD group had poorer sleep efficiency and longer sleep latency on most days than the reference group. The SWD group reported lower sleep quality and less relaxation at bedtime across all days. KSS sleepiness was greater in the SWD group than in the reference group at the beginning of morning shifts, at the end of morning shifts, and at the end of night shifts. The SWD group also showed more PVT lapses at the beginning of night shifts than the reference group.

Conclusions: The ICSD-3 criteria produced lower SWD prevalence estimates than the ISCD-2 criteria. Many employees only sporadically experienced primary symptoms of SWD, which is not consistent with ICSD criteria. To reduce the amount of false positive SWD cases, future studies should not diagnose these individuals as having SWD. In addition to night shifts, sleep and alertness are also disturbed in SWD related to morning shifts. On days off, SWD was associated with less compensatory sleep and higher prevalence of excessive sleepiness, which implies that individuals with SWD may have reduced capacity to recover from shift work. Further studies are needed to determine whether longer recovery periods could alleviate SWD symptoms.

TIIVISTELMÄ

Johdanto: Suomessa yli 20 % työvoimasta altistuu vuorotyölle tai epäsäännöllisille työajoille. Moni heistä kokee vuorotyöaikatauluun liittyvää unettomuutta ja/tai voimakasta väsymystä/uneliaisuutta. Kansainväliset tautiluokitusjärjestelmät tuntevat ilmiön vuorotyöunihäiriönä. Häiriön kriteerit päivitettiin Kansainvälisen unihäiriöluokituksen kolmannessa painoksessa (*International Classification of Sleep Disorders*, ICSD-3) vuonna 2014. Häiriötä tutkivat tieteelliset julkaisut perustuvat kuitenkin pääosin vanhoihin ICSD-2-kriteereihin. Vuorotyöunihäiriön tieteellisessä tutkimuksessa käytettyjen seulontamenetelmien välillä on huomattavia eroja. Lisäksi ne perustuvat subjektiivisiin mittareihin. Häiriön yleisyydestä huolimatta sen ilmeneminen tunnetaan huonosti tavallisessa arjessa. Ei myöskään tiedetä parantuvatko vuorotyöunihäiriön oireet vapaapäivien aikana. Tämän työn tarkoituksena oli selvittää kuinka erilaiset vuorotyöaikataulut ja vuorotyöunihäiriön seulontamenetelmät vaikuttavat arvioihin häiriön yleisyydestä. Lisäksi tavoitteena oli kartoittaa häiriön ilmenemistä eri työvuoroihin ja vapaa-aikaan liittyen.

Menetelmät: Tutkimus pohjautuu kahteen erilliseen aineistokokonaisuuteen; 1) sairaalahenkilöstön keskuudessa vuonna 2015 toteutettuun "Työajat kuntasektorin henkilöstön seurantatutkimuksessa" (*Working Hours in the Finnish Public Sector*, WHFPS) -poikkileikkauskyselyyn ja siihen yhdistettyyn työaikarekisteriaineistoon sekä 2) lentoaseman maahenkilöstön keskuudessa toteutettuihin kyselyihin ja kolmen viikon kenttätutkimukseen.

Sairaalahenkilöstö (n = 4831) luokiteltiin työaikarekisteritiedon perusteella vuorotyöntekijöiksi, jotka eivät tee yötyötä; työntekijöiksi, jotka tekevät yötyötä tai jatkuvaa yötyötä tekeviksi. Vuorotyöunihäiriö määritettiin yksilötasolla kulloistenkin kriteerien perusteella yhdistämällä seulontakyselyn vastaukset työaikarekisterin tietoihin. Häiriön yleisyys arvioitiin neljää päällekkäistä mukaanottorajaa käyttäen (≥ 1, ≥ 3, ≥ 5 ja ≥ 7 kuukausittaista päivätyöstä poikkeavaa työvuoroa, jossa työskennellään ainakin osittain klo 18:00 ja 06:00 välillä). Lisäksi sairaalatyöntekijät vastasivat kysymyksiin vapaapäivinä esiintyvästä unettomuudesta ja voimakkaasta väsymyksestä/uneliaisuudesta sekä tyypillisestä vuorokausittaisesta unen määrästä.

Kyselyvastausten perusteella lentokentän maahenkilöstöstä 22 luokiteltiin vuorotyöunihäiriöryhmään ja yhdeksän vertailuryhmään. Kyselyn lisäksi univalverytmiä tarkkailtiin kolmen viikon ajan unipäiväkirja- ja aktigrafiaseurannalla. Tähän kenttämittausjaksoon sisältyi myös etukäteen määrättyjä aamu- ja yövuoropäiviä sekä vapaapäiviä, joiden aikana osallistujat arvioivat uneliaisuuttaan (*Karolinska Sleepiness Scale*, KSS), tekivät vireystilaa mittaavia reaktioaikatestejä (*Psychomotor Vigilance Test, PVT*) sekä tallensivat untansa aivosähkökäyrään pohjautuvalla menetelmällä.

Tulokset: ICSD-3-kriteereihin perustuvan vuorotyöunihäiriön yleisyys sairaalahenkilöstössä vaihteli mukaanottorajasta riippuen 3 - 4 % välillä yötyötä sisältämättömässä vuorotyössä, 3 - 10 % välillä yötyötä sisältävässä vuorotyössä ja oli 6 % jatkuvassa yötyössä. Häiriö oli merkitsevästi yleisempää ICSD-2- kuin ICSD-3-kriteerien perusteella, vaihdellen 7 - 9 % välillä yötyötä sisältämättömässä vuorotyössä, 6 - 34 % välillä yötyötä sisältävässä vuorotyössä sekä ollen 17 % jatkuvassa yötyössä. Häiriö oli merkitsevästi yleisempää yötyötä sisältävässä kuin sitä sisältämättömässä vuorotyössä, kun mukaanottorajana käytettiin ≥ 1 tai ≥ 3 kuukausittaista päivätyöstä poikkeavaa työvuoroa.

ICSD-2 -kriteereihin perustuva vuorotyöunihäiriö oli sairaalahenkilöstössä positiivisesti yhteydessä voimakkaaseen väsymykseen/uneliasuuteen vapaapäivinä ja negatiivisesti yhteydessä unettomuuteen vapaapäivinä. Myös häiriön alaluokka, jossa vuorotyöaikatauluun liittyy unettomuutta (mutta ei voimakasta väsymystä/uneliaisuutta), oli yhteydessä voimakkaaseen väsymykseen/uneliaisuuteen vapaapäivinä sekä lisäksi pienempään vuorokautiseen unen määrään.

Lentokentän maahenkilöstön kenttätutkimuksessa vuorotyöunihäiriöryhmä ilmoitti ennen aamuvuoroja nukkuvansa vähemmän ja kärsivänsä suuremmasta univajeesta kuin vertailuryhmä. Toisin kuin vertailuryhmä, vuorotyöunihäiriöryhmä näytti vapaapäivinä nukkuvan vain vähän yli unentarpeensa. Vuorotyöunihäiriöryhmällä oli useimpina päivinä myös merkitsevästi tehottomampi uni ja pidempi nukahtamisviive kuin vertailuryhmällä. Päivästä riippumatta vuorotyöunihäiriöryhmä arvioi rentoutumisensa ennen nukkumaanmenoa vähäisemmäksi ja unenlaatunsa heikommaksi kuin vertailuryhmä. Vuorotyöunihäiriöryhmän KSS-uneliaisuus oli vertailuryhmää voimakkaampaa aamuvuorojen alussa ja lopussa sekä yövuorojen lopussa. Lisäksi yövuorojen alussa vuorotyöunihäiriöryhmässä ilmeni enemmän hitaita PVT-reaktioaikoja kuin vertailuryhmässä.

Johtopäätökset: Vuorotyöunihäiriön yleisyys jäi ICSD-3-kriteereillä pienemmäksi kuin ICSD-2 -kriteereillä. Monella sairaalatyöntekijällä ilmeni lisäksi vain harvoin vuorotyöunihäiriön oireita, mikä ei ole ICSD:n vuorotyöunihäiriökriteerien mukaista. Väärien positiivisten määritysten välttämiseksi tulevissa tutkimuksissa tälle joukolle ei pitäisi diagnosoida vuorotyöunihäiriötä. Yövuorojen lisäksi uni ja vireys näyttävät vuorotyöunihäiriössä häiriintyvän myös aamuvuorojen yhteydessä. Vapaapäivinä häiriö oli yhteydessä vähäisempään korvausuneen ja yleisempään voimakkaaseen väsymykseen/uneliaisuuteen, mikä voi kieliä heikommasta kyvystä palautua vuorotyöstä. Tulevissa tutkimuksissa tulisi selvittää, helpottaisivatko pidemmät työvuorojen väliset vapaajaksot vuorotyöunihäiriön oireita.

CONTENTS

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on two separate sets of data, the epidemiological Working Hours in the Finnish Public Sector (WHFPS) study data (Studies I and II) and the shift work disorder field study data (Study III). The results have been reported in the following original publications (I–III), which are referred to in the text by their Roman numerals. In addition, some unpublished data are presented.

I Vanttola P, Puttonen S, Karhula K, Oksanen T, Härmä M (2020) Prevalence of shift work disorder among hospital personnel: A cross-sectional study using objective working hour data. *J Sleep Res* 29(3):e12906. DOI: 10.1111/jsr.12906

II Vanttola P, Puttonen S, Karhula K, Oksanen T, Härmä M (2020) Employees with shift work disorder experience excessive sleepiness also on non-work days: a cross-sectional survey linked to working hours register in Finnish hospitals. *Ind Health* 58(4):366–374. DOI: 10.2486/indhealth.2019-0179

III Vanttola P, Härmä M, Viitasalo K, Hublin C, Virkkala J, Sallinen M, Karhula K, Puttonen S (2019) Sleep and alertness in shift work disorder: findings of a field study. *Int Arch Occup Environ Health* 92(4):523–533. DOI: 10.1007/s00420-018-1386-4

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ABBREVIATIONS

AASM	American Academy of Sleep Medicine
APA	American Psychological Association
CI	Confidence interval
dl	Decilitre
DSM-5	The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
ESS	Epworth Sleepiness Scale
EU	European Union
FPS	Finnish Public Sector
HUS	Hospital District of Helsinki and Uusimaa
IARC	International Agency for Research on Cancer
ICD-10	The 10th revision of the International Statistical Classification of Diseases and Related Health Problems
ICD-11	The 11th revision of the International Classification of Diseases
ICSD-2	The second edition of the International Classification of Sleep Disorders
ICSD-3	The third edition of the International Classification of Sleep Disorders
ILO	International Labour Organization
IQR	Interquartile range
κ	Cohen’s kappa
KSS	Karolinska Sleepiness Scale
LMM	Linear mixed model
ms	Millisecond
MSLT	Multiple Sleep Latency Test
MWT	Maintenance of Wakefulness Test
N1	Non-rapid eye movement, stage 1
N2	Non-rapid eye movement, stage 2
N3	Non-rapid eye movement, stage 3
NREM	Non-rapid eye movement
OR	Odds ratio
OSA	Obstructive sleep apnoea
PSG	Polysomnography
PVT	Psychomotor Vigilance Test
REM	Rapid eye movement
RLS	Restless legs syndrome
s	Second
SD	Standard deviation
SS-Q	Shift-specific questions on insomnia and sleepiness
SSS	Stanford Sleepiness Scale

SWD	Shift work disorder
SWD-Es	Shift work disorder subtype with excessive sleepiness only
SWD-I	Shift work disorder subtype with insomnia only
SWD-IEs	Shift work disorder subtype with both insomnia and excessive sleepiness
SWA	Slow wave activity
SWS	Slow wave sleep
TST	Total sleep time
USA	United States of America
WHFPS	Working Hours in the Finnish Public Sector
WHO	World Health Organization

1 INTRODUCTION

The functioning of the modern 24/7-society depends on the contribution of shift workers. Healthcare, the service industry, transportation, and manufacturing all rely on shift workers (International Agency for Research on Cancer, IARC 2020), i.e., individuals who work outside a regular daytime schedule (06:00/07:00–18:00 hours) to enable extended operation of an establishment (Monk and Folkard 1992; International Labour Organization, ILO 2004). In the European Union (EU) (Eurofound 2017), as well as in Finland (Sutela et al. 2019), approximately every fifth worker works shifts.

The misalignment of the individuals' and the environment's rhythms affects sleep, alertness, performance, and attention. Shift work disturbs sleep and causes sleepiness, especially in relation to night and early morning shifts (Åkerstedt and Wright 2009). Many shift workers perform their duties when the body would be ready for rest, and this has negative effects on health.

Sleep preserves the normal physiological processes of the body and has a strong impact on health and well-being (Van Someren et al. 2015). Sleep affects metabolic, hormone, and immune system regulation (Mullington et al. 2010; Van Someren et al. 2015), learning and memory (Hobson 2005), mood, and vigilance (Van Someren et al. 2015). Sleep also alters the circadian rhythms of core clock gene expression and the genes related to inflammatory, immune, and stress responses (Van Someren et al. 2015).

Among shift workers, restorative sleep, re-entrainment, and recovery support health and wellbeing, whereas sleep deprivation, circadian disruption, and increased activation lead to disturbed health (Merkus et al. 2015). Meta-analyses and systematic reviews have linked shift work to health problems such as acute sleep loss, occupational accidents and injuries, weight gain, type 2 diabetes, coronary heart disease, stroke, and breast, prostate, and colorectal cancers, although studies are somewhat inconsistent (Kecklund and Axelsson 2016). In addition, shift workers are at risk of developing shift work disorder (SWD), a chronic circadian rhythm sleep-wake disorder characterised by insomnia, excessive sleepiness, or both (the American Academy of Sleep Medicine, AASM 2005, 2014; World Health Organization, WHO 2019a). The major coding manuals of disorders state that these primary symptoms of SWD must be associated with a shift work schedule that overlaps conventional sleep time (AASM 2005, 2014; American Psychological Association, APA 2014; WHO 2019a).

In the literature, the prevalence rate of SWD has typically been estimated using the second edition of the International Classification of Sleep Disorders (ICSD-2) criteria for SWD (AASM 2005). Approximately 20%—30% of shift workers have screened positive for ICSD-2-based SWD, although SWD prevalence estimates have varied between 3% (Rajaratnam et al. 2011) and 63% (Taniyama et al. 2015). This reflects the diversity of the study populations, the composition of shift schedules, and the SWD screening methods used. The coding manuals do not define cut-off values for the occurrence of shifts or SWD symptoms. Nor do they give a particularly specific definition of SWD symptoms. As a result, studies have defined SWD using different methods, which complicates comparison between them.

Although the diagnosis of SWD is recognised by the major disorder coding manuals (AASM 2014; APA 2014; WHO 2019a), it is not widely used in clinical settings (Culpepper 2010). Based on epidemiological studies, certain working-time features, such as a greater number of night shifts and < 11-hour intervals between work shifts, increase the risk of SWD (Flo et al. 2014; Waage et al. 2014). However, in real life, the manifestation of SWD has only been studied in permanent night work (Gumenyuk et al. 2014; Gumenyuk et al. 2015), and little is known about how SWD manifests in relation to different naturalistic work shifts in shift work. Indeed, more mechanistic studies using the latest ICSD diagnostic criteria for SWD have been called for to expand the knowledge on SWD and its prevalence in shift-working populations (Wright et al. 2013).

In this thesis, I use the most current version of the ICSD to define SWD, ICSD-3. The thesis focuses on elucidating how shift work schedules and SWD definitions affect the prevalence estimates of SWD. I also focus on the day-to-day variation of SWD manifestation in a naturalistic setting and on the success of recovery from SWD on days off in field and epidemiological settings. In the literature review, I present sleep as the primary daily rhythm of the body, describe how sleep and alertness are regulated and measured, and introduce insomnia and sleepiness both in general and in the context of shift work. I also review the literature on the characteristics and health effects of shift work, recovery from shift work, and ICSD-based SWD.

2 REVIEW OF THE LITERATURE

2.1 CIRCADIAN RHYTHMS AND SLEEP

We have adapted to the diurnal fluctuation of our rotating planet. The intrinsic circadian (24-hour) rhythms of our bodies keep us active during the daytime and resting at night-time. The rhythms of, for example, hormone secretion and temperature, follow the rhythms of our environment by keeping track of external zeitgebers, such as light and temperature (Dallmann et al. 2016). The level of sleepiness coincides with these rhythms, peaking at around 05:00 hours (nadir of alertness), when body temperature is at its minimum (Czeisler et al. 1980). The body's melatonin concentration is at its maximum between approximately 02:00 and 04:00 hours (Czeisler et al. 1980; Benloucif et al. 2008; Scholtens et al. 2016).

Melatonin is one of the primary circadian hormones that promote sleep. The suprachiasmatic nucleus (SCN) of the hypothalamus controls the secretion of melatonin from the pineal gland through clock gene expression (Herzog 2007). Light detected by the photoreceptors of the retina entrains SCN activity through the retinohypothalamic tract. Light inhibits and darkness stimulates the synthesis and secretion of melatonin during the night (Dallmann et al. 2016).

The human biological night typically includes the period from 23:00 to 07:00 each night (IARC 2020). However, the timing of sleep depends on individual circadian rhythms, for example, due to the chronotype — phase of entrainment in relation to zeitgebers (Roenneberg and Merrow 2007) — and can vary due to cultural differences, for instance (IARC 2020). Circadian rhythms are essential for living, and their disruption affects health and well-being negatively (Brainard et al. 2001; Vetter 2020).

The sleep–wake cycle follows circadian rhythmicity. Sleep is a state of immobility and reduced consciousness which preserves vitality and the ability to function during wakefulness. Although the ultimate function of sleep is unresolved, synaptic plasticity and higher-order cognitive functions, such as learning and memory, depend on sleep (Porkka-Heiskanen et al. 2013; Frank and Heller 2019). For example, insufficient sleep impairs vigilance and performance (Van Dongen et al. 2003). In addition, sleep regulation and immune responses are connected. For example, pro-inflammatory cytokines promote and anti-inflammatory molecules inhibit sleep. Sleep has been found to boost the immune system and improve recovery from infections (Porkka-Heiskanen et al. 2013). Reciprocally, poorer sleep can predispose an individual to, for example, the common cold (Cohen et al. 2009). On the other hand, sleep serves as a restorative 'housekeeping' process that removes metabolic waste and maintains brain energy metabolism and macromolecular biosynthesis (Porkka-Heiskanen et al. 2013; Frank and Heller 2019).

2.1.1 SLEEP MEASURES

Sleep can be evaluated using different methods such as polysomnography (PSG), actigraphy (i.e., accelerometry), sleep diaries, or questionnaires. The concurrent use of different methods can be useful, as each method measures slightly different dimensions of sleep. For example, subjective experiences form the basis of many sleep disorder diagnoses, whereas objective methods can verify or provide insight into the condition (AASM 2014; APA 2014; WHO 2019a).

PSG is a golden standard diagnostic method to study sleep architecture and diagnose sleep disorders such as sleep apnoea, periodic limb movement disorder, and narcolepsy. The measurements are typically carried out in a laboratory during an overnight stay. The main PSG methods include electroencephalography (EEG), which records cortical activity; electromyography (EMG), which records muscle activity; and electrooculography (EOG), which records eye movements. Their profiles are used to score sleep stages epoch by epoch (Iber et al. 2007).

Whereas PSG measures brain surface activity, actigraphy measures movements, usually from the non-dominant wrist. Immobility is defined as sleep. Actigraphy shows over 90% agreement in total sleep time (TST) with PSG. However, actigraphy may underestimate sleep onset latency or waketime after sleep onset and overestimate sleep efficiency, i.e., the percentage of time actually spent sleep of the time spent in bed (Ancoli-Israel et al. 2003). The advantage of actigraphy over PSG is that actigraphy is cost-effective and can easily be used for long periods outside laboratory. Thus, it is convenient in field studies that last from days to weeks. Actigraphy is typically used together with a sleep diary, in which individuals indicate at least their sleep start and end times and, depending on the study, also other evaluations of their sleep and wakefulness. PSG is the primary method for diagnosing many sleep–wake disorders, but the AASM, for example, requires that a SWD's disturbed sleep–wake pattern should be demonstrated by a ≥ 14-day sleep diary and actigraphy monitoring (AASM 2014).

Although individuals typically overestimate their sleep time (Lauderdale et al. 2008), self-reported habitual sleep correlates moderately with actigraphy-measured sleep length (Kwok et al. 2018). Epidemiological studies use self-evaluations, from single questions to questionnaires, to measure sleep (Lauderdale et al. 2008). A self-evaluation is a useful and cost-effective method for obtaining information from a large group of people. In general, validated questionnaires on sleep length or sleep difficulties, such as the Jenkins Sleep Problem Scale (Jenkins et al. 1988), the Pittsburgh Sleep Quality Index (Buysse et al. 1989), the Bergen Insomnia Scale (Pallesen et al. 2008), and the Karolinska Sleep Questionnaire (Nordin et al. 2013), are preferred over single-item questions as they can capture the target phenomenon more precisely. For example, sleep length showed better correlation with actigraphy measures when it was calculated from evaluations of bedtime, waketime and sleep latency than self-reported sleep length (St-Onge et al. 2019).

2.1.2 STRUCTURE OF SLEEP

Based on PSG measures, vigilance states can be classified into wakefulness, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep. NREM is further classified into three stages: N1, N2, and N3 sleep — or light sleep (including N1 and N2 sleep) and slow wave sleep (SWS, including N3 sleep) (Iber et al. 2007).

During wakefulness, EMG shows muscle activity and EEG is dominated by low amplitude fast frequency (8–13 Hz) alpha waves, although 4–8 Hz theta and > 13 Hz beta waves, for example, can also be detected. In the transition from wakefulness to sleep, the synchrony of neural oscillation gradually increases while muscle activity and consciousness decrease. Sleep deepens from N1 sleep (dominated by low-amplitude mixed frequency theta waves) and N2 sleep (including theta waves with K complex or 11–16 Hz sleep spindle) to SWS. SWS is characterised by < 4 Hz delta waves, and is scored when > 20% of the epoch consists of high amplitude (> 75 µV) and low frequency (0.5–2.0 Hz) slow wave activity (SWA) in the frontal region. SWS is followed by REM sleep, characterised by rapid eye movement, muscle atonia — and much like wakefulness — a mixture of low amplitude and high frequency brain waves (e.g. theta and alpha) (Iber et al. 2007).

The cycle of light sleep, SWS, and REM sleep recurs approximately every 90 minutes throughout a sleep period. SWS is associated with recovery, and prolonged wakefulness increases its intensity. SWS is especially prevalent during the first part of sleep and typically fades away towards the end of a sleep period as the proportion of REM and light sleep increases (Borbély 1982; Scammell et al. 2017).

2.1.3 TWO-PROCESS MODEL OF SLEEP REGULATION

According to the two-process model of sleep regulation, the interplay between a circadian process and a homeostatic process regulates sleep propensity (Borbély 1982). The circadian process functions as a pacemaker for sleep, increasing propensity for sleep at night-time and decreasing it during the daytime. The circadian process follows the time of day in accordance with an endogenous circadian SCN oscillator that is entrained by cues from the environment, mainly light (Borbély 1982; Porkka-Heiskanen et al. 2013; Borbély et al. 2016). Melatonin and core body temperature rhythms serve as typical circadian sleep propensity markers (Czeisler et al. 1999). The homeostatic process keeps track of time spent awake and asleep by, for example, following the level of extracellular adenosine in the basal forebrain (Porkka-Heiskanen et al. 2013). The homeostatic process increases sleep pressure due to sleep debt or prolonged wakefulness and reduces sleep pressure during sleep. Increased SWA and SWS during sleep are used as homeostatic sleep propensity markers (Borbély 1982; Porkka-Heiskanen et al. 2013).

In addition to Borbély's (1982) model, which has a single circadian oscillator, to simulate circadian behaviour, models with more than one oscillator have been proposed. For example, the two interacting oscillator (Kronauer et al. 1982) and the three-oscillator (Kawato et al. 1982) models describe the human circadian system through an interplay between the oscillators that control the core body temperature rhythm and the sleep-wake cycle. In these mathematical models, the former affects the latter more than vice versa.

Generally, increased sleep pressure appears as intensified SWA, longer sleep, and better-quality sleep (Borbély 1982; Porkka-Heiskanen et al. 2013; Borbély et al. 2016). In addition, since EEG theta activity increases during prolonged wakefulness, for example during night shifts (Torsvall and Åkerstedt 1987; Kecklund and Åkerstedt 1993), it can be regarded as a marker of homeostatic sleep pressure during waketime (Finelli et al. 2000).

2.1.4 AMOUNT OF SLEEP AND INDIVIDUAL FACTORS

The amount of habitual sleep (Banks and Dinges 2007) and sleep need (Ferrara and De Gennaro 2001; Polo-Kantola et al. 2016) vary considerably from one individual to another. Sleep need refers to the duration of sleep needed to not feel sleepy during the daytime (Banks et al. 2017). The National Sleep Foundation (the United States of America, USA) recommends between seven and nine hours of sleep for healthy adults (Hirshkowitz et al. 2015). Laboratory studies suggest that favourable sleep length varies between 8.2 and 8.9 hours among young adults and is approximately 7.4 hours among the elderly (Van Dongen et al. 2003; Klerman and Dijk 2008).

Sleep dept typically means increased sleep pressure due to an insufficient amount of physiologically normal sleep (Banks et al. 2017). Social or working life demands can cause sleep debt by causing an individual to sleep insufficiently for one or multiple nights, which can be referred to as partial sleep restriction (Van Dongen et al. 2003; Klerman and Dijk 2008; Banks et al. 2017). Sleep debt can also result from acute total sleep deprivation, when, for example, a night shift keeps a worker awake for the whole night or even longer, as in some experiments (Van Dongen et al. 2003; Banks et al. 2017). Based on epidemiological studies, and thus subjective evaluations, seven to eight hours of habitual sleep supports health. Outside this range, the risk of mortality and morbidity grows (Hublin et al. 2007; Cappuccio et al. 2010; Yin et al. 2017; Kwok et al. 2018; Garcia-Perdomo et al. 2019).

Many individual and environmental factors modulate sleep. Older age is associated with less sleep, longer sleep latency, decreased sleep efficiency, greater sleep fragmentation, nocturnal awakenings, more wakefulness after sleep onset, less SWS, more light sleep, and earlier bedtime and wake-up time (Ohayon et al. 2004; Boulos et al. 2019). REM sleep has shown to be impaired among elderly people, similarly as in neurodegenerative disorders (Ohayon et al. 2004; Mander et al. 2017).

Women report a longer sleep need (Ursin et al. 2009; Polo-Kantola et al. 2016) and sleep longer (Ursin et al. 2009) than men. In the Finnish population, self-estimated sleep length was 7.4 hours for women and 7.3 hours for men in 2017 (Partonen et al. 2018). Chronotype can also affect sleep (Fabbian et al. 2016) in the context of work schedules, for example. After night shifts, early chronotypes (preference for earlier wake-up and bedtime) can have shorter sleep and higher levels of sleep disturbance than later chronotypes (preference for later wake-up and bedtime). A similar pattern can also be seen before morning shifts, but among the opposite chronotypes. (Juda et al. 2013; Hittle and Gillespie 2018). Older adults tend to have an earlier chronotype than younger adults (Roenneberg and Merrow 2007). Women are typically described as having an earlier chronotype than men; but the opposite has also been shown, particularly with increasing age (Merikanto et al. 2012; Randler and Engelke 2019). Light environment can also affect the perceived chronotype within a population (Roenneberg and Merrow 2007).

2.1.5 INSOMNIA

In Finland, the Current Care Guidelines (Duodecim 2020) define symptoms of insomnia in accordance with the definitions of insomnia disorders in the major disorder coding manuals – the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10, F51.01/F51.02) (WHO 2019b), the 11th revision of the International Classification of Diseases (ICD-11, 7A00/01/0Z) (WHO 2019a), ICSD-3 (AASM 2014), and the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, 307.42) (APA 2014) – as difficulty initiating or maintaining sleep (AASM 2014; APA 2014; WHO 2019a, b), waking up earlier than desired (AASM 2014; APA 2014; WHO 2019b), or unsatisfactory quality of sleep (APA 2014; WHO 2019a, b). Further, the Current Care Guidelines define insomnia disorder according to ICD-10 as difficulty initiating or maintaining sleep or as non-restorative sleep that occurs ≥ 3 times a week for at least one month and is associated with worry or impaired daytime functioning in daily life.

Symptoms of insomnia and sleepiness, although not necessarily clinically severe, are common in the general population. According to epidemiological studies, approximately every third individual reports insomnia symptoms (Ohayon and Partinen 2002; Leger et al. 2008), while 6%–19% may fulfil the diagnostic criteria for chronic insomnia (Ohayon and Partinen 2002; Riemann et al. 2017). Furthermore, 24% of the Finnish population (Partonen et al. 2018) and 21% of the Norwegian population (Ursin et al. 2009) have insufficient sleep.

In general, women more often report symptoms of insomnia than men (Groeger et al. 2004; Zhang and Wing 2006; Ursin et al. 2009; Partonen et al. 2018; Fetveit et al. 2019). In addition, the symptoms of insomnia increase with age (Pandi-Perumal et al. 2002; Fetveit et al. 2019) and poorer health

(Rosekind and Gregory 2010; Morin et al. 2015; Fetveit et al. 2019). Furthermore, stress can affect sleep through the hypothalamus-pituitary-adrenal axis that secretes hormones such as the corticotropin-releasing hormone, the adrenocorticotropic hormone, and cortisol, which also promote wakefulness (Steiger 2002; Bonnet and Arand 2010). In modern society, psychosocial stress is a common cause of insomnia (Elovainio et al. 2009; Kompier et al. 2012; Fetveit et al. 2019).

2.1.6 SLEEPINESS AND FATIGUE

Sleepiness can be described as a subjective drive towards sleep that is reciprocal to alertness (Dement and Carskadon 1982). Both the Stanford Sleepiness Scale (SSS) (Hoddes et al. 1973) and the Karolinska Sleepiness Scale (KSS) (Åkerstedt and Gillberg 1990) are widely used one-item situational sleepiness measures. The SSS is a seven-point scale from 1 (feeling active, vital, alert, or wide awake) to 7 (no longer fighting sleep, sleep onset soon; having dream-like thoughts) in which scoring ≥ 3 signifies ‘sleepy’. The KSS is a nine-point scale from 1 (extremely alert) to 9 (extremely sleepy, great effort to keep awake, fighting sleep). KSS was used in Study III of this thesis. Physiological intrusions of sleep in the EEG/EOG typically start at level 7 on the KSS and dominate EEG-recordings at level 9. KSS levels of 5–6.5 can be regarded as high and levels of 4–4.5 as intermediate levels of sleepiness, while KSS levels of < 4 can be regarded as normal alertness levels (Åkerstedt and Wright 2009; Åkerstedt et al. 2014).

Another widely used subjective sleepiness scale is the Epworth Sleepiness Scale (ESS) (Johns 1991). Its items assess the likelihood of dozing off in different daytime situations. The ESS is used to measure general-level daytime sleepiness (excessive sleepiness cut-off at ESS ≥ 10). Thus, it may not be ideal for assessing sleepiness during shift work, since unlike the KSS or SSS, it is not a situational sleepiness measure (Johns 1991, 1992; Åkerstedt and Wright 2009).

Physiological sleepiness is typically measured objectively in a sleep laboratory by means of the Multiple Sleep Latency Test (MSLT). In the MSLT, the individual tries to fall asleep and their sleep latency is determined by the EEG in four 20-minute session at two-hour intervals. The naps are ended as soon as they start. Sleep latency of < 5 minutes represents a pathological level, latency of 5–10 minutes an intermediate level, and latency of > 10 minutes a low level of physiological sleepiness (Åkerstedt and Wright 2009). Typical nocturnal sleep latency can range between three and seven minutes (Richardson et al. 1982; Buysse et al. 2005; Gumenyuk et al. 2012). The maintenance of Wakefulness Test (MWT) is another method for assessing excessive sleepiness. The MWT is similar to the MSLT; however instead of trying to sleep, individuals are asked to try to stay awake. Sleep latency of < 10 minutes indicates excessive daytime sleepiness (Mitler et al. 1982).

In the lack of consensus, the scientific community has developed numerous measures for fatigue (Harrington 2012), and despite the attempts of the literature to define sleepiness and fatigue, these definitions sometimes partially overlap. For example, a single-item question on sleepiness or fatigue may include different dimensions of sleepiness, fatigue, or tiredness, and only the participants of each study know what dimension(s) they were thinking of when they answered the question. Sleepiness refers to propensity for sleep and is usually regulated by recent sleep and circadian rhythms, while fatigue also has physical and mental components including tiredness (Mullins et al. 2014). Shen et al. (2006) define fatigue as *an overwhelming sense of tiredness, lack of energy and a feeling of exhaustion, associated with impaired physical and/or cognitive functioning*. Both sleepiness and fatigue can impair task performance. However, these impairments can be reversed through different mechanisms: sleepiness by sleeping and fatigue by discontinuing the task that caused the fatigue (Balkin and Wesensten 2011; Mullins et al. 2014). Another distinction between the two could be that whereas sedentary activity and rest can exacerbate sleepiness, they may reduce fatigue (Åkerstedt and Wright 2009).

2.1.7 ALERTNESS AND VIGILANT ATTENTION

Much like the two-process model of sleep regulation explains changes in sleep propensity over 24 hours, the three-process model of alertness uses the circadian and homeostatic processes, in addition to the sleep inertia process, to describe daily fluctuations of alertness (Åkerstedt and Folkard 1997). Due to the circadian process, staying awake and alert is easiest during daytime and most difficult at night-time. Due to the homeostatic process, alertness decreases, and sleepiness increases as wakefulness is extended. Due to sleep inertia, alertness is depressed on awakening and improves gradually, approximately within 15–30 minutes (Hilditch and McHill 2019). Sleep stage affects the ease of awakening, waking up being easiest from N1 sleep and most difficult from SWS (Scammell et al. 2017). Sleep inertia can be a huge challenge for those on on-call duty who must awaken close to the nadir of alertness and be able to function immediately after waking (Ferguson et al. 2016; Hilditch et al. 2016).

Sleep restriction can result in neurobehavioral deficits, such as performance deficits and attention lapses. Both chronic sleep restriction (e.g., < 7 hours of sleep per night for several days) and acute total sleep deprivation can decrease alertness and cause sleepiness and cognitive dysfunction (Van Dongen et al. 2003; Banks and Dinges 2007; Goel et al. 2013). Like alertness and sleepiness, vigilant attention is also affected by the circadian, homeostatic, and sleep inertia processes. This has been demonstrated using psychomotor vigilance tests (PVT) (Monk et al. 1997; Mollicone et al. 2010; Hudson et al. 2020).

The PVT is a reaction time task in which an individual responds as quickly as possible to a visual stimulus that appears at a random interval (2–10 seconds, s). Typically, performance outcomes in PVT include mean reaction time and number of lapses of attention (reaction times of > 500 milliseconds, ms) (Dinges and Powell 1985). Interestingly, after sustained sleep restriction, vigilant attention appears to return to baseline level more slowly than self-estimated sleepiness. This is thought to result from an allostatic process (Karatsoreos and McEwen 2011), which adjusts homeostatic regulation based on sleep-wake history over previous days or weeks (Hudson et al. 2020). In allostasis, the organism actively adapts to the changing environment through physiological changes (Karatsoreos and McEwen 2011).

2.2 SHIFT WORK – WORKING AGAINST ONE'S BIOLOGICAL RHYTHMS

In addition to circadian and homeostatic regulation and sleep inertia, environmental factors due to, for example, shift work or flying over time zones also regulate the fluctuation of sleep propensity, alertness, timing of sleep, and the sleep-wake pattern. To support the functioning and structures of modern society, shift workers must perform duties when the body is prepared for rest. Shift work affects approximately every fifth worker's life in Finland (Kandolin and Tuomivaara 2013; Sutela et al. 2019), in the EU (Eurofound 2017), and in the USA (Wickwire et al. 2017). Shift work is especially common in transportation, healthcare, manufacturing, and the service industry (IARC 2020).

According to the European Commission (2003) and the ILO (ILO 2004), shift work is a method for organising work in shifts, so that workers succeed one another at the same workstations to enable longer operation over days or even weeks. Shift arrangements can extend work to the whole 24 hours of the day by alternating different individuals or teams (IARC 2020). The scientific literature on working hours often defines shift work as any work outside 06:00/07:00–18:00 hours (Monk and Folkard 1992; Caruso 2014), which is consistent with this thesis.

2.2.1 DIFFERENT SHIFT TYPES

Work shifts are defined by their timing. Common shift types include morning, day, evening, and night shifts, but their definitions vary. For example, ILO defines night work as a ≥ 7-hour work period including the period from 00:00 to 05:00 hours (ILO 1990a, b), whereas the EU defines it as ≥ 3 hours of work at *night-time* (as defined by national law) including the period from 00:00 to 05:00 hours (European Commission 2003). Finnish law defines night-time as the period between 23:00 and 06:00 hours (Ministry of Justice 2020). In this thesis, a night shift is defined as ≥ 3 hours of work between 23:00 and 06:00

hours. Garde et al. (2019) have also used this definition. Overall, a night shift includes work during the conventional sleeping hours of the general population, for example, between 23:00 and 08:00 hours (Wright et al. 2013; IARC 2020). Further, a morning shift usually starts between 04:00 and 07:00/08:00 hours and an evening shift includes work between 14:00 and 24:00 hours (Wright et al. 2013; IARC 2020). A shift work schedule can also include day shifts, i.e., work between 06:00/07:00 and 18:00 hours (Monk and Folkard 1992).

2.2.2 SHIFT ARRANGEMENTS

Work shifts can be arranged in multiple ways. IARC (2020) lists the main features of shift work. Shift work can be organised with or without night shifts (including whole or part of the night). Shift system can be continuous (include every day of the week) or discontinuous (include, for example, only weekdays). It can be permanent (composed of only one shift type) or rotating (shift type regularly changes to another). Shift systems can rotate forward or backward, and depending on the length of the shift cycle, rotation can be fast or slow. In a forward rotating system, the next shift starts ≥ 24 hours after the start of the previous shift, for example — in order — morning shift, evening shift, night shift. A fast cycle can last only one week. In a slowly forward rotating system, the same shift type can occur several times before a change to a later shift type. In a backward rotating system, the next shift starts ≤ 24 hours after the start of the previous shift (e.g., in order: night shift, evening shift, morning shift). The number of different shift types varies only slightly between individuals within a regular shift system, whereas in an irregular shift system the shift type changes to another irregularly and shift composition varies within and between individuals. Irregular work schedules are common in the healthcare sector, for example. The length of individual shifts typically varies between eight and twelve hours but can be shorter or longer. The number of consecutive shifts varies depending on the placement of days off. In addition, the number and length of recovery period between shifts and shift cycles can vary (Sallinen and Kecklund 2010; IARC 2020).

Typical eight-hour shift work systems include three-shift schedules (with night shifts), two-shift schedules (with or without night shifts), and permanent night work schedules. Various compressed work schedules with extended shifts (for example, 14 consecutive workdays with 12-hour shifts) also exist (Sallinen and Kecklund 2010; IARC 2020).

2.2.3 ADJUSTMENT TO SHIFT WORK

The circadian rhythm typically adjusts slowly, approximately one hour per 24 hours (Wever 1980; Folkard et al. 1991; Folkard 2008). Adjustment to a new time zone succeeds with the help of natural light as a zeitgeber. Social and physical activities and eating times can also enhance adjustment (Carskadon et al. 2004). However, adjustment to a shift work schedule may not be as smooth due to fluctuations in the timing of shifts and opposing zeitgebers of the environment, for example, natural light in the morning after a night shift or activities on days off (Åkerstedt 2003).

2.2.3.1 Effects of work shifts and schedules

Different work shifts affect sleep and alertness in different ways. To prepare for being awake at work, shift workers often sleep longer or nap prior to the first night shift (Åkerstedt 2003). Nevertheless, sleepiness is common in night shifts (Härmä et al. 2002; Åkerstedt and Wright 2009) and employees may involuntarily fall asleep during them (Åkerstedt et al. 2002; Åkerstedt and Wright 2009; Vedaa et al. 2019). Performance is also affected at night-time, and night shifts have been associated with accidents, injuries, and errors (Åkerstedt and Wright 2009; Larsen et al. 2017; Nielsen et al. 2018; Vedaa et al. 2019; Härmä et al. 2020).

Night shifts — and evening shifts to a lesser extent — postpone bedtime (Åkerstedt 2003; Åkerstedt and Wright 2009). Employees typically start sleeping one hour after the night shift ends and fall asleep quickly, in less than five minutes. Despite increased homeostatic sleep pressure, the sleep period may be one to four hours shorter than normal due to decreased circadian sleep propensity during daytime (Åkerstedt and Wright 2009). In addition to premature awakening, other symptoms of insomnia can also occur after a night shift (Flo et al. 2013). Those with early chronotype in particular sleep less after a night shift (Juda et al. 2013). The amount of REM and N2 sleep decreases, whereas the amount of SWS is less affected (Dahlgren 1981; Torsvall et al. 1989; Åkerstedt et al. 1991), which has also been shown in laboratory settings after sleep restriction (Webb and Agnew 1965; Van Dongen et al. 2003). Even so, acute total sleep deprivation studies indicate that middle-aged adults may get less efficient sleep with less SWS during a daytime recovery sleep period than younger adults (Gaudreau et al. 2001; Lafortune et al. 2012). Although awakening occurs naturally, employees perceive sleep after a night shift as insufficient, and can compensate for it by napping in the afternoon (Åkerstedt 2003; Åkerstedt and Wright 2009).

Sleep length and the amount of REM and N2 sleep may also be shortened prior to a morning shift (Åkerstedt 2003). However, sleep quality may remain unaffected. Early awakening in particular shortens sleep among those with late chronotype (Juda et al. 2013). Since sleep is typically cut short before a morning shift, homeostatic and circadian sleep pressure have not completely disappeared upon awakening. Thus, shift workers typically perceive sleep before a morning shift as unrefreshing. Like night shifts, morning shifts are also associated with sleepiness. Early awakening causes sleep debt and sleepiness during the day, and it is common to nap after the shift in the afternoon (Åkerstedt 2003; Åkerstedt and Wright 2009).

In addition to separate shift types, the composition of a shift work system and the length of a recovery period between shifts also affect sleep (Knauth and Hornberger 2003; Flo et al. 2014). It has been suggested that slowly rotating shift schedules reduce sleep length less than separate night shifts or fast rotating shift schedules (Pilcher et al. 2000; Åkerstedt and Wright 2009). On the other hand, the amount of consecutive night shifts in the roster and the employees' ability to adjust to night work can crucially impact the overall amount of sleep. A recent study showed that sleep duration did not increase along with an increasing amount of consecutive night shifts, but instead led to the build-up of sleep debt (Garde et al. 2020). Further, backward rotation has more clearly been associated with disrupted sleep than forward rotation, probably because an individual's circadian clock tends to be slow (Driscoll et al. 2007; Åkerstedt and Wright 2009).

Both shift work with night shifts and permanent night work are associated with night shift-related insomnia and sleepiness. Insomnia problems seem to be more prevalent among rotating night shift workers than among permanent night workers, probably due to greater fluctuation in the timing of work and greater homeostatic sleep pressure during night shifts among the former than the latter (Flo et al. 2013). Permanent night work enables partial entraining of circadian rhythms to the work schedule (Wilkinson 1992). However, individuals commonly shift towards a diurnal routine on their days off (Wedderburn 1992; Folkard 2008). Among Norwegian nurses at least, the risk of insomnia symptoms on days off appears to be higher in permanent night work than in rotating night shift work (Flo et al. 2013). In fact, only every fifth permanent night worker appears to be able to sufficiently adjust endogenous melatonin rhythm to night work (Folkard 2008). Overall, night shifts increased the risk of insomnia (odds ratio, OR 1.48, 95% confidence intervals, CI 1.10–1.99) and chronic fatigue (OR 1.78, 95% CI 1.02–3.11), among the Norwegian nurses, but not the risk of excessive daytime sleepiness (OR 1.27, 95% CI 0.90–1.80) (Øyane et al. 2013).

Backward rotating shift schedules, two- or three-shift schedules, and irregular shift schedules can include short (< 11-hour) recovery periods (EU 2003) between shifts, most often after an evening shift. These short shift intervals — or quick returns — are often associated with shortened or disturbed sleep and increased sleepiness or fatigue (Knauth and Hornberger 2003; Vedaa et al. 2016; Vedaa et al. 2017; Härmä et al. 2018). In addition, quick returns have been associated with accidents (Vedaa et al. 2019; Vedaa et al. 2020) and injuries (Nielsen et al. 2018), for instance.

2.2.3.2 Recovery from shift work

Recovery supports health and wellbeing (Geurts and Sonnentag 2006). According to the effort-recovery model (Mejman and Mulder 1998), normal work-related load reactions (activation of psychophysiological systems) may develop into chronic load reactions, such as fatigue and sleep difficulties, if exposure to workload is constant and recovery is incomplete. The model describes recovery as a psychophysiological unwinding to a stabilised baseline level of activation, which can be achieved in the absence of special demands (Mejman and Mulder 1998; Geurts and Sonnentag 2006).

Allostasis maintains homeostasis of the body through separate psychophysiological (or allostatic) systems. Allostatic load theory lists the autonomic nervous system, the hypothalamic-pituitary-adrenal axis, the metabolic systems, and the immune system as relevant for recovery (McEwen 1998; Geurts and Sonnentag 2006). Based on the theory, lack of recovery can cause chronic activation of the allostatic systems, which disturbs the homeostatic balance of the body and may thus predispose the body to diseases (McEwen 1998; Geurts and Sonnentag 2006). Circadian disruption due to shift work can alter allostasis and elevate allostatic load (McEwen and Karatsoreos 2015). Consistently with this, heart rate variability may fluctuate according to a shift work schedule (Järvelin-Pasanen et al. 2013; Jensen et al. 2016; Goffeng et al. 2018), and immune status may (Puttonen et al. 2011; Wirth et al. 2017; Loef et al. 2019) or may not (Copertaro et al. 2011; Buss et al. 2018) react to shift work exposure.

Geurts and Sonnentag (2006) describe incomplete recovery as a mechanism underlying the connection between acute physiological stress reactions and chronic health impairment (such as prolonged fatigue and sleep difficulties). They summarise that "*recovery is a process of psychophysiological unwinding after effort expenditure*."

Recovery from stressful work characteristics may be internal or external. Internal recovery refers to opportunities to recover during working time, for example, during coffee breaks or during naps on night duty (Geurts and Sonnentag 2006). Consuming caffeine, bright light exposure, or taking a short nap can also improve alertness and performance (Caldwell et al. 2019; Ritonja et al. 2019). External recovery takes place between work shifts or while on a holiday, and — in addition to sleep — can be composed of 'true' free time of a passive or active nature, or domestic activities or other obligatory chores (Geurts and Sonnentag 2006).

On a general level, days off are associated with longer sleep than workdays (Tepas and Carvalhais 1990; Groeger et al. 2004). During workdays, sleep length can be 20–45 minutes shorter than on days off (Groeger et al. 2004; Swanson et al. 2011; Petersen et al. 2017). In addition, subjective sleep quality appears to decline on workdays (Groeger et al. 2004). A similar difference in self-assessed sleep length, approximately 40 minutes, has been found between workdays and holidays (de Bloom et al. 2013). These findings concerning longer sleep on days off than on workdays correlate with the homeostatic process of the two-process model of sleep regulation, in which sleep deprivation increases sleep propensity, and according to Borbély (1982), is followed by recovery sleep.

In shift work, unsuccessful recovery is associated with fatigue, sleepiness, and sleep difficulties (Sallinen and Kecklund 2010; Kecklund and Axelsson

2016). Shift work interferes with circadian sleep regulation and increases the need for recovery from work (Jansen et al. 2003). Besides, shift work challenges recovery by making shift workers balance between work and social activities (Kandolin and Huida 1996; Puttonen et al. 2010; Drach-Zahavy and Marzuq 2013). This makes efficient recovery particularly important for shift workers.

Sleepiness is common among shift workers on days off (Åkerstedt et al. 2000). The risk of fatigue/tiredness on days off decreased when healthcare workers of Finnish hospitals transferred from shift to day work (Härmä et al. 2019) and increased when the prevalence of non-day shifts (night and evening shifts) increased (Härmä et al. 2018). Interestingly, the risk of long sleep also decreased as healthcare workers transferred from shift to day work (Härmä et al. 2019) and increased when the prevalence of non-day shifts increased (Härmä et al. 2018). Reports of long sleep probably stem from an increased need for recovery from shift work, representing Borbély's (1982) recovery sleep, and can thus be regarded as a sign of an individual's adaptation to the disturbed sleep pattern related to shift work schedules. Although sleep length typically decreases in relation to night and morning shifts, average sleep length (covering also evening shift days and days off) can increase, which may be beneficial for shift workers. For example, laboratory studies have shown that sleep extension (in comparison to habitual sleep time) for one week before sleep restriction sustained performance and objective alertness during the days of sleep restriction and improved recovery (Rupp et al. 2009; Arnal et al. 2015).

One night's recovery sleep has shown to be insufficient for full neurobehavioral recovery after chronic partial sleep restriction (4–5 hours of sleep per night for ≥ 5 days) in laboratory settings (Dinges et al. 1997; Banks et al. 2010; Haavisto et al. 2010). Similarly, a study of nurses showed incomplete recovery from two consecutive night shifts after one day off in terms of maintaining wakefulness, performance, and executive function (Chang et al. 2018). However, subjective sleepiness showed similar levels among those recovering from night shifts and those recovering from day shifts. Interestingly, recovery of performance — measured by PVT — appears to be slower than recovery from self-estimated sleepiness (Dinges et al. 1997; Belenky et al. 2003; Axelsson et al. 2008; Pejovic et al. 2013; Hudson et al. 2020). Field study findings indicate that shift workers need at least two recovery nights (or three consecutive days off) after night shifts to recover from subjective sleepiness (Totterdell et al. 1995; Åkerstedt et al. 2000) or fatigue (Haluza et al. 2019).

2.2.4 SHIFT WORK DISORDER

Individuals are different in their vulnerability to shift work, extended working hours, and sleep loss (Härmä 1993; Van Dongen and Belenky 2009). Shift workers can develop chronic shift schedule-related insomnia and/or excessive sleepiness, that is, SWD. SWD is included in ICSD-3 in the category of circadian rhythm sleep-wake disorders (AASM 2014). Although SWD is an under-recognised diagnosis in the clinical setting (Culpepper 2010), SWD diagnosis can be utilised in, for example, occupational healthcare to improve shift workers' health. However, currently, SWD diagnosis cannot be reliably detected in registers for the purpose of, for example, population-based studies. Moreover, the diversity of the methods used to screen SWD (Table 1) makes it difficult to compare the observed results of studies. Due to the limited data available on SWD, Wright et al. (2013) called for more mechanistic studies using the most current ICSD diagnostic criteria for SWD to improve comprehension of the disorder and to further elucidate its prevalence among shift working populations.

Saksvik-Lehouillier et al. (2015) found that a person's physical health and well-being (including mental health and social functioning) were important individual factors among nurses for adapting to shift work. A systematic review among healthcare workers suggests that older age, early chronotype, low circadian flexibility in sleeping habits, neuroticism, low hardiness (resilience to stress and illness), being married, having children, and increased caffeine consumption may be associated with vulnerability to SWD or sleep-related impairment in response to shift work, whereas physical activity may be a protective factor (Booker et al. 2018). As for studies on SWD, they have shown mixed evindence regarding associations between SWD and chronotype. Depending on the population, SWD has been associated with later chronotype (Flo et al. 2012; Asaoka et al. 2013; Di Milia et al. 2013; Waage et al. 2014; Booker et al. 2020a), neither chorotype (Waage et al. 2009; Taniyama et al. 2015), or earlier chronotype (Chen et al. 2020).

Another review identified organisational factors such as recurrent quick returns, recurrent or extended night shifts, recurrently missing nap opportunities during night shifts, and unhealthy workplaces (lack of improvement processes to protect and promote the health, safety, and well-being of workers through collaboration between workers and managers; Burton 2010) as determinants of SWD, excessive sleepiness, or insomnia (D'Ettorre et al. 2018). These factors can vary widely depending on jobs and workplaces. For example, aviation is a sector in which rest requirements are carefully regulated to inhibit fatigue-related risks (European Commission 2014).

2.2.4.1 Definitions of SWD

According to ICSD-2 (AASM 2005) and ICSD-3 (AASM 2014) criteria, SWD is a circadian rhythm sleep-wake disorder characterised by insomnia, excessive sleepiness, or both, resulting from a prolonged shift work schedule that recurrently at least partially overlaps the conventional night-time sleep period. ICD-11 (7A64) (WHO 2019a) and DSM-5 (307.45) (APA 2014) refer to SWD as a circadian rhythm sleep-wake disorder, shift work type. The primary symptoms of SWD, i.e., insomnia and/or excessive sleepiness, should not be better explained by other disorders, medication, or poor sleep hygiene (AASM 2005, 2014). In Finland, the Current Care Guidelines (Duodecim 2020) classify SWD, (or insomnia caused by shift work or shift work insomnia) according to ICD-10 (G47.26 and Z57.8), under sleep-wake disorders that are explicitly caused by an environmental factor. SWD can be categorised into three subtypes on the basis of its primary symptoms as follows: both insomnia and excessive sleepiness (Rajaratnam et al. 2011; Barger et al. 2015; Gumenyuk et al. 2015), insomnia only, and excessive sleepiness only (Gumenyuk et al. 2015).

The ICSD criteria for SWD were updated in 2014. The revised edition, ICSD-3 (AASM 2014), adds to primary symptoms a reduction of TST as an accompanying symptom of SWD. In comparison, ICD-11 states that SWD is *typically* associated with a reduction in TST. Further, compared to ICSD-2, ICSD-3 has increased the minimum manifestation period of the SWD symptoms from at least one to at least three months. DMS-5 refers to the former as episodic SWD and the latter as persistent SWD (APA 2014). To demonstrate a disturbed sleep-wake pattern, compared to ICSD-2, ICSD-3 increased actigraphy and sleep diary monitoring from one to two weeks (AASM 2005, 2014). However, it is not known whether transferring from the former to the current ICSD criteria influences, for example, the prevalence of SWD.

As the coding manuals define SWD in slightly different ways, and as they do not specify cut-off values for frequency of shifts or SWD symptoms, studies have defined SWD in various ways, typically using the ICSD-2 criteria. To make easier the comparison of findings of this thesis and previous research, I refer to the ICSD-2 criteria of SWD in relation to ICSD-based SWD research when the reduction of TST has not been considered as a criterion for SWD even though ICSD-3 may have been mentioned. (Table 1)

Waage et al. (2009) developed three dichotomous questions that evaluate whether potential sleeping difficulties or experiences of excessive sleepiness are associated with a work schedule that overlaps the conventional sleep period for at least one month. Rajaratnam et al. (2011) developed a series of questions that evaluate whether insomnia (based on the Athens Insomnia Scale) (Soldatos et al. 2000) and/or excessive sleepiness (difficulties with sleepiness or likelihood of dozing off/falling asleep) in connection with night shifts decrease on days off or during daytime. Further, Barger et al. (2012) developed and validated a four-item SWD screening questionnaire which includes items on insomnia (problems waking up too early and not being able to get back to sleep), impaired well-being (sense of well-being), and excessive sleepiness (likelihood of dozing off at work) in relation to shift work during the past month and sleepiness (likelihood of dozing off/falling asleep while driving) after at least two days off from work. These three approaches associate the primary symptoms of SWD with shifts, at least partially. Some other SWD

Table 1 *SWD prevalence according to work schedule and definition of SWD used in different studies.*

Author (year)	Study population[A] [response rate, mean age, females]	Study design	Definition of SWD in relation to ICSD-2-criteria I and/or Es symptoms, SOS, R, and additional criteria	Prevalence of SWD, % (n) Permanent day shifts	Shift work without night shifts	Shift work with night shifts	Other schedule with night work	Permanent night shifts
Drake et al. (2004)	2570 adults, Detroit tricounty, USA [70%, 40 yrs, 48%]	Cross-sectional telephone survey	*ICSD Revised (AASM 2001) was used to define SWD.* *i.*• **I:** Difficulty falling asleep/staying asleep/nonrestorative sleep (≥ 1 mth, ≥ 'sometimes' over lifetime, and self-reported severity ≥ 6/10 over past 3 mths) • **Es:** Excessive daytime sleepiness (ESS > 13) • **SOS**: - • **R**: Self-reported work schedule during past 2 wks	18% (≈ 351)		26% (≈ 88)		32% (≈ 52)
			ii. As *i* minus the SWD prevalence in D workers (18%) in *i*	0% (0)		8% (≈ 27)		14% (≈ 23)
Waage et al. (2009)	103 oil rig workers, Norway [79% (n = 204[B]), 39–42 yrs, 5%]	Cross-sectional survey	• **I** or **Es**: Difficulties sleeping or excessive sleepiness • **SOS**: I or Es is related to a shift work schedule ≥ 1 mth • **R**: Swing shifts: 2-wk work (7 D, 7 N), 4-wk non-work				23% (24)	
Rajaratnam et al. (2011)	1861 police officers with ≥ 1 N during past mth, North America [n = 4957[B]: -, 39 yrs, 17%]	Cross-sectional prospective online cohort and onsite cohort	*i.*• **I** and **SOS**: Insomnia after N (Athens Insomnia Scale, AIS ≥ 6), but not on days off/holiday (AIS < 6) • **Es** and **SOS**: a. Greater likelihood of dozing off/falling asleep while driving after N than while driving after ≥ 2 days off from work; b. greater likelihood of dozing off/falling asleep during N than during D/E; and/or c. greater sleepiness difficulties while on N schedule than while on vacation/days off • **R**: ≥ 3 N during past mth, self-reported				54% (1004)	
			*ii.*as *i*, plus both '**I** and **SOS**' and '**Es** and **SOS**' must occur				15% (269)	
			*iii.*as *i*, plus both '**I** and **SOS**' and wake-time drowsiness and **SOS** (a. ≥ moderate chance of falling asleep while driving after N compared with ≤ slight chance on days off; and b. ≥ moderate chance of falling asleep during N compared with ≤ slight chance during D)				3% (47)	
Swanson et al. (2011)	67 resident adult, employed ≥ 30 h/week, USA [n = 1000[B]: 17%, 47 yrs, ≈ 45%]	Cross-sectional telephone survey	• **I:** a. Difficulty with sleep onset/maintenance or early morning awakenings ≥ a few nights/wk and b. daytime sleepiness interferes with functioning ≥ a few days/wk • **Es:** Excessive daytime sleepiness (ESS ≥ 10) • **SOS**: - • **R**: work starts between 18–06 hours, self-reported			21% (14)		

i–iii: Flo et al. (2012) *iv–vi:* Eldevik et al. (2013) *vii:* Waage et al. (2014)	1990 nurses, Norway, working ≥ 17.8 h/wk (or ≥ 18.8 h/wk if permanent D) [T0 (n = 2059[B]): 38%, 33 yrs, 90%; T1 (n = 1533): 79%, -, 91%]	Cross-sectional (*i–vi*) / longitudinal (*vii*) cohort (2008/2009 and 2011)	*i.* As Waage et al. (2009) • **R**: self-reported work schedule; mean 2 N & 3 QR/mth	6% (9)	29% (137)	44% (488)	41% (22)	44% (70)
			ii. In addition to *i*: exclusion of cases with symptoms of OSA, RLS, periodic limb movement and parasomnias based on the Global Sleep Assessment Questionnaire	5% (7)	28% (131)	43% (472)	41% (22)	43% (68)
			iii. In addition to *i*: Bergen Insomnia Scale scores above clinical cut-off or ESS ≥ 11	6% (8)	25% (117)	39% (425)	38% (20)	34% (53)
			iv. In addition to *i*: 0 QR/yr	25% (≈ 71)				
			v. In addition to *i*: 1–30 QR/yr	35% (≈ 256)				
			vi. In addition to *i* > 30 QR/yr	45% (≈ 402)				
			vii. In addition to *i*: inc. also those 2.8% working < 17.8 h/wk	T0: 36% (538), T1: 29% (433), both T0 & T1: 19% (281)				
Asaoka et al. (2013)	997 nurses, University hospitals, Tokyo, Japan [81% (n = 1202[B]), 30 yrs, 100%]	Cross-sectional survey	As Waage et al. (2009) • **R**: shift worker; mean 11 D & 4 N/mth or 14 D & 3 E & 3 N/mth, self-reported			20% (≈ 61)	26% (≈ 182)	
Di Milia et al. (2013)	1163 workers from general population, 3 cities, Australia [50%, 45 yrs, 54%]	Cross-sectional telephone survey	Almost as Waage et al. (2009) except: *i.*•**SOS**: I or Es symptom must be related to work schedule, but not to *shift* work schedule • **R**: self-reported work shifts	10% (≈ 90)		32% (≈ 85)		
			*ii.*In addition to *i*: **I** or **Es** symptom very negatively affects person's social, family, or work relationships	1% (≈ 12)		9% (≈ 24)		
Barger et al. (2015)	5771 firefighters from 66 fire departments, USA [n = 6933[B]: ≈ 38%, 40 yrs, 6%]	Cross-sectional cohort	As the *ii.* definition of Rajaratnam et al. (2011) • **R**: ≥ 1 N during past mth, ≈ 81% had ≥ 24-hour shifts, self-reported			9% (525)		
Kalmbach et al. (2015)	96 normally sleeping D/E workers or un-employed (T0), South-eastern Michigan, USA [T0: -, 39 or 48 yrs, 63%]	Longitudinal prospective cohort	Consistent with Drake et al. (2004) with some changes: • **I:** Difficulty initiating/maintaining sleep or having non-restorative sleep ≥ 1 mth and sleep problem interferes with daily functioning ≥ somewhat • **Es:** Excessive daytime sleepiness (ESS ≥ 10) • **SOS**: **I** and/or **Es** temporally corresponded with transitioning to rotating shift work at 1-year follow-up • **R**: self-reported work schedule			19% (18)		

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Author (year)	Study population[A] [response rate, mean age, females]	Study design	Definition of SWD in relation to ICSD-2-criteria I and/or Es symptoms, SOS, R, and additional criteria	Prevalence of SWD, % (n)				
				Permanent day shifts	Shift work without night shifts	Shift work with night shifts	Other schedule with night work	Permanent night shifts
Taniyama et al. (2015)	Manufacturing industry workers, Japan [82% (n = 556[B]), 40 yrs, 0%]	Cross-sectional survey	As Waage et al. (2009) *i.*•**R**: rapidly rotating shifts ≈ 9 D & 9 N/mth			63% (228)		
			ii. In addition to *i*, **I** and/or **Es** is always unpleasant			39% (≈ 142)		
Kerkhof (2018)	250 citizens of the Netherlands [-, 39 yrs, ≈ 48%]	Cross-sectional online research panel-based survey	• **I:** 'The Holland Sleep Disorders Questionnaire - Insomnia criterion' (Kerkhof 2017) • **Es:** Excessive daytime sleepiness: Falling asleep involuntarily, especially in monotonous situations • **SOS**: - • **R**: self-reported shift work schedule	8% (≈ 79)	12% (≈ 31)			
Booker et al. (2020b) Booker et al. (2020a)	202 nurses, Austin Hospital, Melbourne, Australia [43%, 35 yrs, 95%]	Cross-sectional survey as part of a clustered randomised controlled trial	Shiftwork Disorder Screening Questionnaire (Barger et al. 2012) was used to define SWD • **I:** Problems waking up too early and not being able to get back to sleep • **Es:** Dozing off at work • Decreased sense of well-being during time awake • **SOS**: *If applicable:* Not dozing off while driving after ≥ 2 days off from work • **R**: mean 9 D & 7 E & 6 N/mth			29% (59)		
Chen et al. (2020)	706 intern nurses before any shift work exposure (T0), Guangzhou, China [T0: -, 18 yrs, 100%; T1: 95%, -, -; T2: 90%, -, -]	Longitudinal prospective cohort [3 (T1) and 6 mths (T2) after transferring to shift work]	• **I:** difficulties falling asleep/difficulties maintaining sleep/waking up too early and not being able to fall asleep again > 3 times/wk during past 3 mths. • **Es:** Excessive daytime sleepiness (ESS ≥ 11) • **SOS**: Sleep or sleepiness problem has been related to shift work schedule ≥ 3 mths • **R**: shift schedule includes D & E or D & E & N		T1: 35% (236), T2: 38% (240), both T1 & T2: 18% (129)			

[A] in which SWD was assessed; [B] inc. individuals not analysed for SWD; yr, year; ≈, approximately; I, Insomnia; Es, Excessive sleepiness; SOS, symptom(s) result from overlap with conventional night-time sleep period; R, recurrence of shift work schedule; M, morning shift; D, day shift; E, evening shift; N, night shift; QR, quick return; mth, month; wk, week.

screening methods assess insomnia and excessive sleepiness among shift workers, but do not connect the symptoms specifically to shift work (Drake et al. 2004; Swanson et al. 2011; Kerkhof 2018). When Flo et al. (2012) combined these two approaches by complementing the definition of SWD based on Waage et al. (2009) with a clinical cut-off for insomnia and excessive daytime sleepiness, the prevalence of SWD was 5% smaller. Some screening methods include a negative daytime consequence as an SWD criterion either as part of the definition of SWD (Swanson et al. 2011; Barger et al. 2012; Kalmbach et al. 2015) or as an additional, more strict definition of SWD (Di Milia et al. 2013). Some studies have also included permanent dayworkers in analyses of shift workers (Di Milia et al. 2013; Eldevik et al. 2013; Waage et al. 2014). The diversity of SWD screening instruments complicates the comparison of studies. There is a lack of knowledge on whether or how the use of different instruments affects study results.

2.2.4.2 Prevalence

The prevalence of SWD has been studied using the ICSD-2 criteria for SWD. For example, the AASM has estimated that SWD prevalence may be 2%–5% in the general population of the USA (AASM 2005). The prevalence varies widely among shift workers, probably reflecting differences between working time patterns, the screening instruments used to identify SWD, occupations, and populations. SWD prevalence rates of up to 54%–63% have been reported (Rajaratnam et al. 2011; Taniyama et al. 2015). The highest rate, 63%, was found among factory workers (all male) in Japan with rapidly rotating shifts; their shift schedule included approximately nine night shifts a month. SWD prevalence was 23% in another male dominant workplace (95% male) with oil rig swing-shift workers in Norway, when the same three-question SWD screening instrument was used as in the study above. The oil rig workers' shift schedule was compressed and comprised two-week work periods with seven long consecutive night shifts offshore and four-week non-work periods (Waage et al. 2009). The SWD prevalence difference between the factory and oil rig workers may partly be explained by the differences in the work schedules and their recovery periods.

SWD prevalence can also vary considerably within an occupation, even if the same SWD screening instrument is used. SWD prevalence was 20%–26% among shift working nurses (all female) in Japan, who had a mean of 3.1–4.5 night shifts a month, when the above three-question SWD screening instrument was used (Asaoka et al. 2013). In comparison, SWD prevalence was higher, reaching 37%, among nurses (90% female) with a mean of two night shifts and a mean of three quick returns per month in Norway (Flo et al. 2012). When the nurses in Norway were grouped on the basis of shift schedule, SWD prevalence rose to 41%–44% among those with night shifts and decreased to 29% among those with only day and evening shifts. Further, when Eldevik et al. (2013) grouped the same cohort of nurses in Norway according to their self-reported occurrence of quick returns, from 0 to > 2.5 per month, SWD prevalence changed from 25% to 45%, respectively.

The composition of the shift schedule can impact the SWD prevalence rate. According to ICSD criteria, the primary symptoms of SWD should be associated with a recurring shift work schedule. However, in irregular shift schedules, some shift workers can have only one or two shifts a month that overlap with conventional night-time sleep, as has been shown by studies based on objective working-hour data of healthcare workers (Härmä et al. 2015; Garde et al. 2019). In these cases, the ICSD criterion of recurrence of shift work may not be fulfilled, and therefore diagnosing SWD may not be relevant. Including those with infrequent shift work may bias SWD prevalence estimates.

Additional SWD criteria to those stated in ICSD-2 have also been used. Rajaratnam et al. (2011) found 54% SWD prevalence among police officers with night shifts in North America using a night shift-based SWD screening tool. When they supplemented the criteria for SWD with the requirement that insomnia had to occur together with a probable chance of falling asleep in connection with a night shift, the prevalence estimate of SWD dropped to 2.5%. Further, based on two longitudinal studies (Waage et al. 2014; Chen et al. 2020), nearly half of those who were initially positive in the screening for SWD were not positive for SWD in the second measurement, which implies that symptoms of SWD tend to fluctuate. Table 1 shows the SWD prevalence studies and their SWD screening criteria in relation to the ICSD-2 criteria.

2.2.4.3 Manifestation of SWD

In line with the SWD criteria, shift workers with SWD have shown to have greater sleepiness (Gumenyuk et al. 2014; Gumenyuk et al. 2015), report more sleep problems (Waage et al. 2009), and evaluate longer sleep latencies (Gumenyuk et al. 2015) than those without SWD in connection with night shift schedules. Shift workers with SWD also appear to report less sleep than shift workers without SWD in connection with night shifts (Gumenyuk et al. 2014; Gumenyuk et al. 2015) and rotating shift work (Kalmbach et al. 2015), although this is not supported by all studies (Di Milia et al. 2013). In addition, a laboratory study using PSG found shorter daytime sleep with poorer sleep efficiency in relation to SWD (Gumenyuk et al. 2010). Sleep diary-based sleep efficiency has shown to be poorer among permanent night workers with SWD than among those without SWD (Gumenyuk et al. 2014; Gumenyuk et al. 2015). SWD appear to be associated with decreased subjective sleep quality among shift workers on a general level (Kalmbach et al. 2015; Taniyama et al. 2015) and among swing-shift workers during a four-week non-work period (Waage et al. 2009). The number of night shifts and quick returns in particular appear to predict SWD among nurses (Flo et al. 2014; Waage et al. 2014). However, how SWD may manifest in relation to morning and evening shifts is not known.

In addition to night shifts and quick returns, daytime sleepiness and depression, but not anxiety, also predicted SWD among nurses (Waage et al. 2014). However, another longitudinal community-based questionnaire study suggested that high sleep reactivity, referring to the sensitivity of an individual's sleep to stress, indirectly increased both depression and anxiety levels through the development of SWD (Kalmbach et al. 2015). Impaired occupational productivity has also been associated with SWD (Belcher et al. 2015). Interestingly, countermeasures such as the use of melatonin and bright light therapy also predicts SWD among nurses (Waage et al. 2014). This may indicate that those with sleeping or circadian rhythm difficulties have failed to find a cure.

Further, SWD has been associated with rigidity in adjusting (i.e., not delaying) the circadian phase to night working hours (Gumenyuk et al. 2012; Gumenyuk et al. 2014; Gumenyuk et al. 2015). Interestingly, a preliminary study found that night workers with SWD were exposed to more morning light, a powerful zeitgeber, than those without SWD (Gumenyuk et al. 2012). In addition, SWD has been associated with cortical hyperarousal (Gumenyuk et al. 2015) and attentional impairment (Gumenyuk et al. 2010; Gumenyuk et al. 2014; Belcher et al. 2015), specifically among permanent night workers whose SWD is only related to insomnia and not to excessive sleepiness.

2.2.4.4 Genetics

Only a few studies — with mixed results — have examined the genetics of SWD. For example, Taniyama et al. (2015) found an association between the *PER1* polymorphism — but not *PER2*, *PER3*, *CRY1*, or *CRY2* — and SWD among shift workers. Gumenyuk et al. (2015) observed preliminary evidence of a genomic predisposition to sleepiness within SWD among permanent night workers who carried the long polymorphism of *PER3*. In contrast, Thun et al. (2016) found no associations between the genetic variants of clock genes (including the above-mentioned genes) and SWD among nurses. Further, Lahtinen et al. (2019; 2021) suggested that SWD and sleep loss may trigger systemic-level loss of DNA methylation, whereas recovery from SWD correlates with restoration of methylation.

2.2.4.5 Treatment

Although different efforts have been made to improve shift workers' circadian adaptation and sleep, SWD still lacks standard treatment options (Wright et al. 2013; Järnefelt et al. 2020). Whole or partial circadian adaptation to a permanent work schedule through properly timed bright light and darkness periods or shifting towards more suitable sleep timing may improve SWD symptoms (Wright et al. 2013). For permanent night workers this could mean exposure to light during night shifts, avoiding light during the commute home, and keeping to a delayed sleep schedule, also on days off. Another treatment approach is to promote sleep. Cognitive behavioural therapy for insomnia may improve insomnia among shift workers (Järnefelt et al. 2012; Peter et al. 2019; Järnefelt et al. 2020). However, those with SWD-type insomnia may benefit from education on sleep hygiene (for example, maintaining as constant as possible a sleep-wake schedule and sleeping in a cool, dark, and quiet environment) and circadian adaptation (Järnefelt et al. 2020). Shift work-related sleep-wake disturbances may also be decreased through organisational efforts such as ergonomic shift scheduling by, for example, decreasing the amount of night shifts (Sallinen and Kecklund 2010; Härmä et al. 2018; Järnefelt et al. 2020) and quick returns (Hakola et al. 2010; Härmä et al. 2018). In addition, alertness during work shifts may be improved using strategic napping before and during a work shift, bright light exposure during a night shift, and consuming caffeine at the beginning of the night shift (Wright et al. 2013; Åkerstedt 2019). In some countries other than Finland, wakefulness-promoting drugs modafinil and armodafinil can be used to treat excessive sleepiness in SWD (Wright et al. 2013).

3 AIMS OF THE STUDY

This study aimed to investigate how the composition of work shifts and the applied definition of SWD affect the estimates of SWD prevalence, and how SWD symptoms manifest and disappear in relation to work shifts and free time. The main aims of this thesis are

1. To estimate the prevalence of SWD among hospital employees in relation to different ICSD-criteria, shift schedules, and the number of non-day shifts (Study I).

2. To objectively and subjectively characterise the day-to-day variation of sleep and alertness in SWD among ground staff in real life (Study III).

3. To explore recovery from SWD on weekly days off (Studies II–III).

4 METHODS

This thesis includes an epidemiological study of hospital employees (Studies I and II) and a field study of airport ground staff (Study III).

4.1 EPIDEMIOLOGICAL STUDY OF HOSPITAL EMPLOYEES (STUDIES I AND II)

4.1.1 STUDY DESIGN AND PARTICIPANTS

In this cross-sectional study, 11 274 employees of six hospital districts in Finland responded to the Finnish Public Sector (FPS) survey (response rate: 69%). Shift scheduling software Titania® (CGI Finland) was used to obtain the employees' realised working hours from a payroll-based register (Härmä et al. 2015). The survey responses were linked to the working hours during the 91 days prior to the survey in 2015.

Hospital employees who, based on the working-hour register, had been exposed to work on at least 31 days (during the 91 days prior to the survey, n = 9 246) were included. Due to missing data on on-call duty, physicians (n = 609) were excluded. To concentrate on fluctuation in circadian rhythm disturbance, permanent day (n = 3 207) and evening (n = 3) workers were excluded. Employees who did not respond to the questions on symptoms of SWD (n = 596) were also excluded. (Figure 1)

In Study I, to explore ICSD-2-based SWD, shift workers without (n = 1 821) and with night shifts (n = 2 926) were classified into four overlapping groups according to minimum cut-offs of ≥ 1, ≥ 3, ≥ 5, and ≥ 7 non-day shifts (work outside 06:00–18:00 hours) per month. As all the permanent night workers (n = 84) had ≥ 7 non-day shifts per month, they comprised one group. Study II focused on shift workers with night shifts who had ≥ 3 non-day shifts per month (n = 2 900). Thus, shift workers without night shifts (n = 1 821), permanent night workers (n = 84), and those with < 3 non-day shifts per month (n = 26) were excluded from Study II. (Figure 1)

In Study I, to explore ICSD-3-based SWD, hospital employees who did not respond to the question on sleep sufficiency (shift workers without night shifts: n = 8, shift workers with night shifts: n = 9) were excluded. Thus, this part of Study I consisted of 1 813 shift workers without night shifts and 2 917 shift workers with night shifts in overlapping groups, as above, and 84 permanent night workers. (Figure 1)

4.1.2 ETHICS

The ethics committee of the Hospital District of Helsinki and Uusimaa (HUS) approved the epidemiological study of hospital employees (Studies I and II) as part of the FPS study (HUS 1210/2016). Each hospital district gave the Finnish Institute of Occupational Health written permission to use their working-hour registry data for scientific research. The data were anonymised for the purpose of the research.

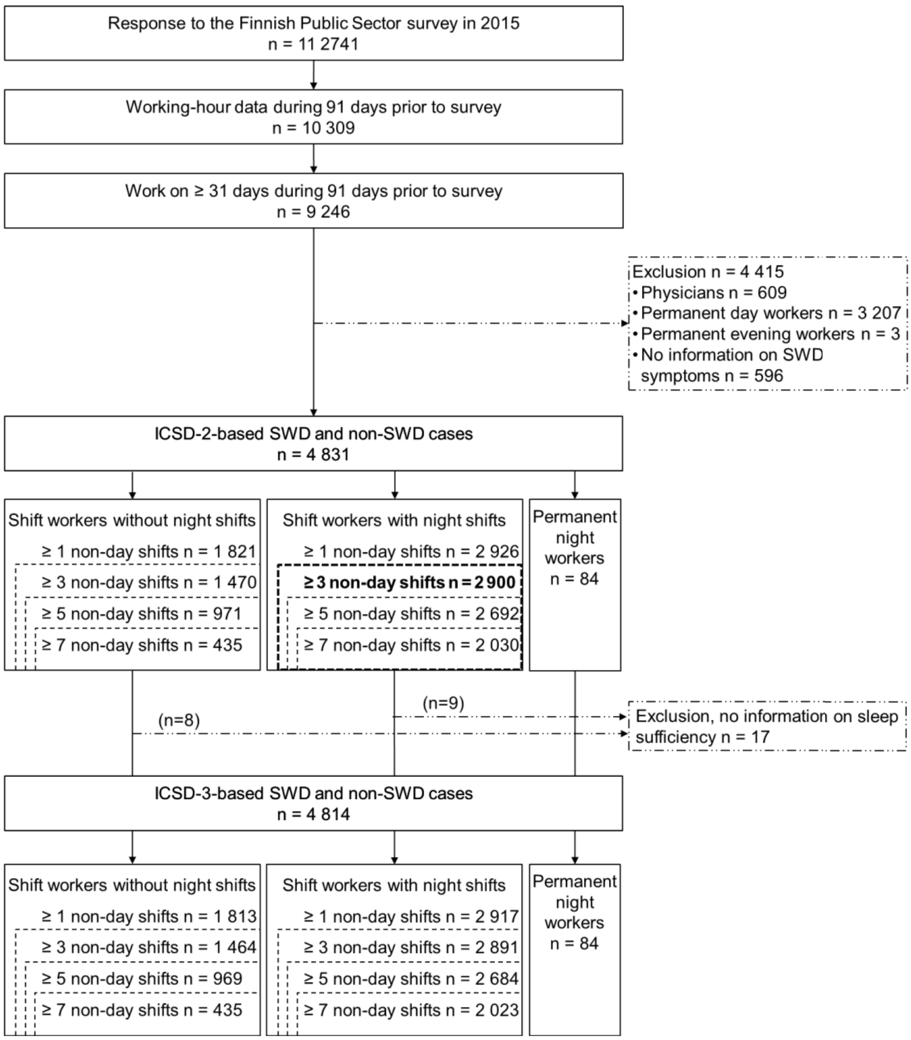

Figure 1 Description of participants in relation to used ICSD criteria and minimum cut-off for non-day (early morning, evening and/or night) shifts (≥ 1, ≥ 3, ≥ 5, ≥ 7 per month) in Study I and Study II (bold).

4.1.3 MEASUREMENTS

4.1.3.1 Register data

In addition to age (year) and sex (man/woman), register data included the start and end times of each hospital employees' shift during the 91 days prior to the survey. Working-hour characteristics were categorised on the basis of these data at the Finnish Institute of Occupational Health for the purpose of the research. Job titles were categorised into healthcare, maintenance, and office/assistant work.

Shift types

Early morning shifts were categorised as shifts starting at 03:00–05:59 and ending 18:00 hours at the latest (Härmä et al. 2015). Morning shifts were categorised as shifts starting at 06:00–08:00 and ending 18:00 hours at the latest. Day shifts were categorised as shifts starting at 08:01 at the earliest and ending 18:00 hours at the latest. Evening shifts were categorised as shifts including work between 18:00–23:00 hours and ending at 01:59 hours at the latest (Härmä et al. 2017). Night shifts were categorised as shifts including ≥ 3 hours of work between 23:00–06:00 hours (Härmä et al. 2015). Early morning, evening, and night shift were grouped together under the category of non-day shifts.

Shift schedules

Study I concentrated on three different shift schedules: shift work without night shifts, shift work with night shifts, and permanent night work. Study II focused on shift work with night shifts. All the shift schedules included work on ≥ 31 days during the 91 days prior to the survey. The schedules were categorised in accordance with Härmä et al.'s (2017) classification: shift work without night shifts included ≥ 1 early morning, morning, and/or day shift, ≥ 1 evening shift, and < 1 night shift per month. Shift work with night shifts included ≥ 1 early morning, morning, and/or day shift, ≥ 1 evening shift, and ≥ 1 night shift per month. Permanent night work included < 1 early morning, morning, or day shift, < 1 evening shift, and ≥ 1 night shift per month.

4.1.3.2 Survey

ICSD-2-based SWD

ICSD-2-based SWD was defined by shift and free time-specific questions on insomnia and excessive sleepiness (Table 2, Studies I and II). First, hospital employees who reported insomnia and/or excessive sleepiness 'never' or 'rarely' while on holiday for more than two weeks and reported the same symptom (insomnia or excessive sleepiness) 'often' or 'always' in connection with morning, evening, and/or night shift (i.e., SWD-related shift types) were classed as survey-based SWD cases. Second, to determine the number of 'days with SWD symptoms', I calculated the number of register-based early morning, evening, and/or night shifts that corresponded to the survey-based SWD-related shift types. Finally, those who had ≥ 1, ≥ 3, ≥ 5 and/or ≥ 7 days with SWD symptoms per month were classed as ICSD-2-based SWD cases in the groups with inclusion cut-offs of ≥ 1, ≥ 3, ≥ 5, and ≥ 7 non-day shifts per month, respectively (Study I).

Study II concentrated on ICSD-2-based SWD with ≥ 3 days with SWD symptoms per month among those with ≥ 3 non-day shifts per month (Figure 1). Based on reports of primary symptoms of SWD (insomnia and/or excessive sleepiness, Table 2), SWD was further categorised into three subtypes (Gumenyuk et al. 2015): SWD subtype with insomnia only (SWD-I), SWD subtype with excessive sleepiness only (SWD-Es), and SWD subtype with both insomnia and excessive sleepiness (SWD-IEs).

Table 2 *Shift and free time-specific questions on insomnia and excessive sleepiness.*

How often during the last three months have you experienced insomnia? By insomnia we mean difficulties initiating sleep, recurrent awakenings during the sleep period, or difficulties staying asleep.

	Never	Rarely	Sometimes	Often	Always	Not applicable
In connection with morning shifts	○	○	○	○	○	○
In connection with evening shifts	○	○	○	○	○	○
In connection with night shifts	○	○	○	○	○	○
On weekly days off	○	○	○	○	○	
While on holiday for > 2 weeks	○	○	○	○	○	

How often during the last three months have you experienced excessive sleepiness?

	Never	Rarely	Sometimes	Often	Always	Not applicable
During morning shifts	○	○	○	○	○	○
During evening shifts	○	○	○	○	○	○
During night shifts	○	○	○	○	○	○
On weekly days off	○	○	○	○	○	
While on holiday for > 2 weeks	○	○	○	○	○	

ICSD-3-based SWD

First, sufficiency of sleep was evaluated using the question 'Do you sleep sufficiently?' with a four-point scale (from 'yes, almost always' to 'rarely or almost never') (Karhula et al. 2018). Then, the ICSD-2-based SWD cases who had ≥ 1, ≥ 3, ≥ 5, and/or ≥ 7 days with SWD symptoms per month and reported having sufficient sleep 'rarely or almost never' were classed as ICSD-3-based SWD cases with ≥ 1, ≥ 3, ≥ 5, and ≥ 7 days with SWD symptoms per month, respectively. (Study I)

Other disorders

The hospital employees responded to the questions 'Has a physician ever told you that you suffer/you have suffered from depression (yes/no), sleep apnoea (yes/no), or restless legs syndrome (RLS, yes/no)?' (Vahtera et al. 2006). (Studies I and II)

Insomnia, excessive sleepiness, and fatigue on weekly days off

Insomnia and excessive sleepiness on weekly days off were evaluated using the sub-questions on weekly days off in Table 2. The hospital employees' responses were dichotomised as 'no' (never/rarely/sometimes) and 'yes' (often/always) (Study II). Fatigue on weekly days off was evaluated using the question 'How often during the last four weeks have you experienced fatigue/tiredness on days off?' with a six-point scale dichotomised as '≤ 1 day off per week' (not at all/on 1–3 days per month/on approximately one day per week) and '≥ 2 days off per week' (on 2–4 days per week/on 5–6 days per week/every day) (Härmä et al. 2017). (Study I)

24-hour sleep length

Subjective 24-hour sleep was evaluated using the question 'How many hours do you normally sleep during 24 hours?' (Vahtera et al. 2006) with a 10-point scale categorised into '≤ 6.5 hours' (≤ 5/6/6.5 hours), '7–7.5 hours' (7/7.5 hours), and '≥ 8 hours' (8/8.5/9/9.5/≥ 10 hours). (Study II)

Chronotype

One question from the Horne and Östbergs' Morningness–Eveningness Questionnaire (1976) was used to evaluate chronotype as follows: 'There are so-called morning types of people (morning spry, evening sleepy) and evening types of people (morning sleepy, evening spry). Which group do you belong to?' Responses on a four-point scale were dichotomised as 'early type' (definitely a morning type/more a morning than evening type) and 'late type' (more an evening than morning type/definitely an evening type). (Studies I and II)

Other background variables

Employees also responded to questions on living with ≥ 1 (< 19-year-old) child (yes/no) (Vahtera et al. 2006; Karhula et al. 2017) and shift work experience (years) (Härmä et al. 2017). (Study II)

4.1.4 STATISTICAL ANALYSES

Analyses were carried out using IBM SPSS Statistics 25.0 (Armonk, New York, USA). P-values under 0.05 indicate statistical significance. Although many analyses were run, the significance level was not set lower, as the number of participants was limited in some analyses. Power calculations were not made before data collection because the hospital employee data were part of an earlier cohort. They were not made later either, because, as Thomas (1997) states, *Calculating power using observed effect sizes is not helpful because such values are very poor estimates of the actual power of the test given the population effect size*.

4.1.4.1 SWD prevalence

An interrelationship of 95% CI was studied to compare the ICSD-2- and 3-based SWD prevalence rates. Pearson chi-squared tests were performed to compare the SWD prevalence rates of shift workers without night shifts and shift workers with night shifts. (Study I)

4.1.4.2 Occurrence of SWD symptoms

The frequency of register-based days with ICSD-3-based SWD symptoms was categorised into < 1 (> 0, < 1), 1 (≥ 1, < 2), 2 (≥ 2, < 3), ... , and 13 (≥ 13, < 14) days with ICSD-3-based SWD symptoms per month. To explore the occurrence of SWD symptoms among the survey-based SWD cases, the mode of days with SWD symptoms per month and the percentage of < 3 days with SWD symptoms per month were calculated among the hospital employees. (Study I)

To suggest a minimum cut-off for SWD symptoms, I compared fatigue on ≥ 2 days off per week (which indicated insufficient recovery from shift work) among SWD cases who had < 3 and ≥ 3, < 5 and ≥ 5, and < 7 and ≥ 7 days with SWD symptoms per month, using Fisher's exact test. (Study I)

4.1.4.3 Recovery from SWD symptoms

To explore recovery from ICSD-2-based SWD on weekly days off and during daily sleep, crude and adjusted logistic regression analyses were performed. Insomnia on weekly days off, excessive sleepiness on weekly days off, and 24-hour sleep length (reference category: ≥ 8 hours) were used as dependent variables. SWD was used as a predictor variable. The adjusted analyses included age, sex, ≥ 1 child, depression, sleep apnoea, and RLS in the model. (Study II)

4.2 FIELD STUDY OF AIRPORT GROUND STAFF (STUDY III)

4.2.1 STUDY DESIGN AND PARTICIPANTS

Between 2012 and 2013, ground staff members at Helsinki Airport (Finland) responded to questionnaires on different occasions and recorded their sleep–wake rhythm for three weeks using actigraphy and a sleep diary. They also took the PVT (Dinges and Powell 1985), rated their sleepiness on the KSS, and recorded sleep using a single channel EEG-based system during predetermined morning shifts, night shifts, and days off. (Figure 2)

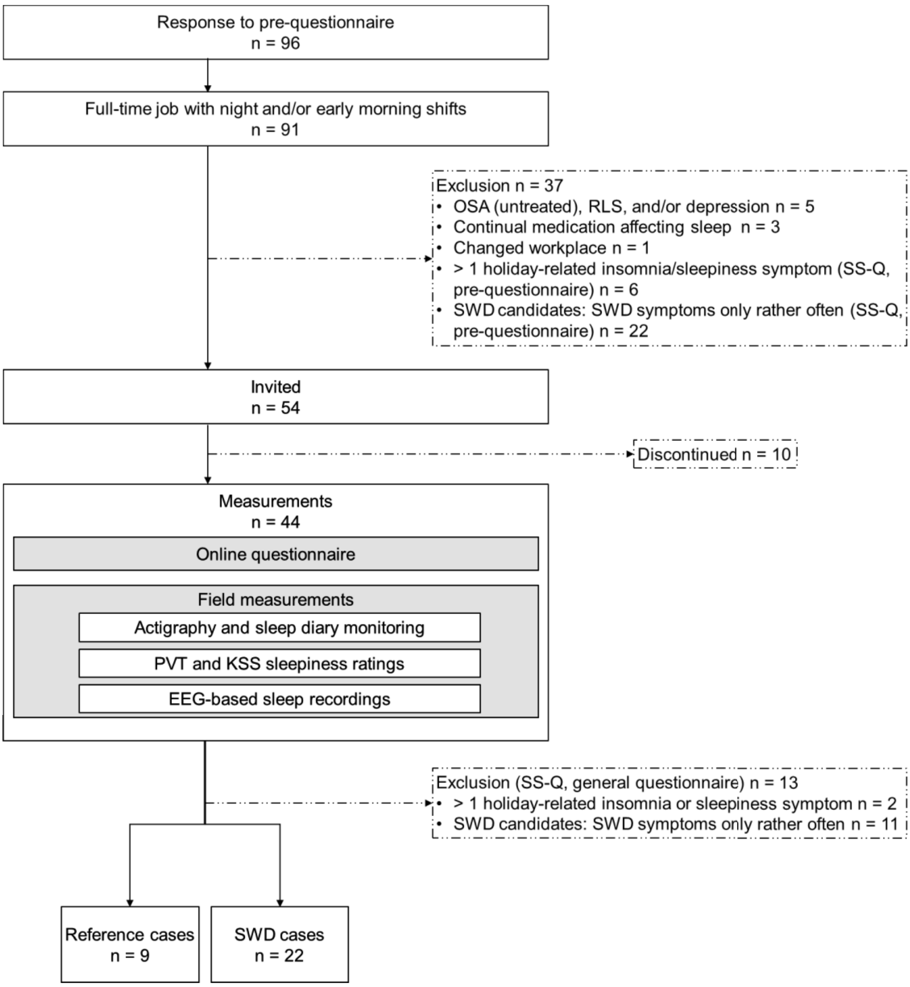

Figure 2 Description of sample in Study III.

A Finnish airline announced this observational field study to the employees of their company, and 96 Helsinki Airport employees in the maintenance, customer service, and catering units volunteered to take part. The ground staff members completed a pre-questionnaire which was used to select volunteers. Full-time employees who had early morning shifts (starting at 03:01–06:00) and/or night shifts (≥ 3 hours of work between 23:00–06:00 hours) in addition to evening shifts (n = 91) fulfilled the working-hour inclusion criteria. Ground staff members with depression, untreated obstructive sleep apnoea (OSA), RLS, or continual medication that affected sleep (n = 8) were excluded. One volunteer who changed workplaces was excluded. Those who based their answers to shift-specific questions on insomnia and sleepiness (SS-Q, Table 3) fell outside the SWD and reference categories were excluded according to predetermined criteria as follows (Figure 2): First, to exclude conditions unrelated to SWD, volunteers with more than one holiday-related insomnia or sleepiness symptom (n = 6) were excluded. Second, to make the interpretation of the results easier, volunteers who were not reference cases, and did not report SWD symptoms sufficiently frequently ('often/continuously') to be classified as SWD cases (n = 22), were excluded (see details in 'SWD' section, page 46).

Fifty-four ground staff members were invited to take part in the study. Ten discontinued. Forty-four employees completed all the measurements for Study III, that is, the online questionnaire and the field measurements. The participants responded again to the SS-Q as part of the online questionnaire in the field study. As the time between responding to the SS-Q as part of the pre-questionnaire and as part of the online questionnaire ranged from weeks to months, and insomnia and sleepiness symptoms can change during such a period, the final classification of the study groups was based on the second responses to the SS-Q. As a result, two more participants with more than one holiday-related insomnia or sleepiness symptom and 11 more SWD candidates with SWD symptoms that only occurred 'rather often' were excluded. Finally, the field study had 22 ground staff members in the SWD group and nine in the reference group. (Figure 2)

4.2.2 ETHICS

The ethics committee of the Hospital District of Helsinki and Uusimaa approved the field study of Helsinki Airport ground staff (Study III, HUS 35/13/03/00/12). Each participant gave their written informed consent. The field study followed the requirements of the Declaration of Helsinki. It was conducted in accordance with the Medical Research Act (488/99) of Finnish law and its later amendments and the Medical Research Decree (986/99) and its later amendments.

4.2.3 MEASUREMENTS

4.2.3.1 Online questionnaire

The ground staff members completed the online questionnaire, which included items on age (years), sex (man/woman), shift work experience (years), smoking (yes/no), OSA (treated with continuous positive airway pressure ≥ 5 hours each night), and chronotype (early/late, identical to the survey item of the hospital employees in Studies I and II) (Horne and Östberg 1976). Flexibility of sleeping habits (scale: 8–40; high scores indicate a tendency towards flexibility) was evaluated using eight items from the Circadian Type Inventory (Barton et al. 1995). The consumption of caffeinated drinks was evaluated by asking 'How many doses of 1) tea (2 decilitres, dl), 2) coffee (1 dl), 3) cola (5 dl), and 4) energy drinks (3.3 dl) do you drink per day?'. Alcohol consumption was evaluated using the question 'How often do you consume alcohol?' with a five-point scale dichotomised as 'no' (never/≤ 1 time per month) and 'yes' (2–4 times per month/2–3 times per week/≥ 4 times per week). Physical exercise was evaluated using the question 'In general, how much do you exercise during your free time?' with a four-point scale dichotomised to 'no' (not so much/walking, cycling, etc. without sweating ≥ 4 hours per week) and 'yes' (≥ 3 hours per week to sustain or improve fitness/several times per week to compete in sports). The ground staff members evaluated their sleep need by reporting the amount of sleep that makes them feel rested the next day.

SWD

The SS-Q was developed to capture the primary symptoms of ICSD-2-based SWD. The SWD and reference groups of the field study were formed on the basis of the answers to the SS-Q as follows (Table 3): The ground staff members had to report insomnia (difficulties initiating sleep, awakening during a sleep period, difficulties falling asleep after awakening, and/or non-restorative sleep) and/or daytime sleepiness 'never/rarely' or 'rather rarely' while on holiday. Those who reported ≥ 1 of the above-mentioned 'never/rarely' or 'rather rarely' occurring symptoms or difficulties staying awake at work 'often/continuously' in connection with morning, evening, and/or night shifts, were classed as SWD cases. Those who reported insomnia and sleepiness 'never/rarely' or 'rather rarely' in connection with all shift types and on holiday were classed as reference cases. Nevertheless, both SWD and reference cases could report one symptom 'rather often' or 'often/ continuously' on holiday. That symptom was not related to SWD.

Table 3 *Shift-specific questions on insomnia and sleepiness (SS-Q).*

How often do you experience difficulties initiating sleep?

In connection with	Never/rarely	Rather rarely	Rather often	Often/continuously	Not applicable
Morning shifts	○	○	○	○	○
Evening shifts	○	○	○	○	○
Night shifts	○	○	○	○	○
Weekly days off	○	○	○	○	
2 weeks on holiday	○	○	○	○	

How often do you awaken during a sleep period?

In connection with	Never/rarely	Rather rarely	Rather often	Often/continuously	Not applicable
Morning shifts	○	○	○	○	○
Evening shifts	○	○	○	○	○
Night shifts	○	○	○	○	○
Weekly days off	○	○	○	○	
2 weeks on holiday	○	○	○	○	

How often do you experience difficulties falling asleep after awakening?

In connection with	Never/rarely	Rather rarely	Rather often	Often/continuously	Not applicable
Morning shifts	○	○	○	○	○
Evening shifts	○	○	○	○	○
Night shifts	○	○	○	○	○
Weekly days off	○	○	○	○	
2 weeks on holiday	○	○	○	○	

How often do you experience non-restorative sleep?

In connection with	Never/rarely	Rather rarely	Rather often	Often/continuously	Not applicable
Morning shifts	○	○	○	○	○
Evening shifts	○	○	○	○	○
Night shifts	○	○	○	○	○
Weekly days off	○	○	○	○	
2 weeks on holiday	○	○	○	○	

How often do you experience daytime sleepiness?

In connection with	Never/rarely	Rather rarely	Rather often	Often/continuously	Not applicable
Morning shifts	○	○	○	○	○
Evening shifts	○	○	○	○	○
Night shifts	○	○	○	○	○
Weekly days off	○	○	○	○	
2 weeks on holiday	○	○	○	○	

How often do you experience difficulties staying awake at work?

In connection with	Never/rarely	Rather rarely	Rather often	Often/continuously	Not applicable
Morning shifts	○	○	○	○	○
Evening shifts	○	○	○	○	○
Night shifts	○	○	○	○	○

Sleep diary and actigraphy monitoring verified disturbed sleep-wake patterns and sleep reduction, as required by ICSD-3, among the SWD cases. In addition, SWD symptoms recurred ≥ 1–2 days per week. The applied definition of SWD is consistent with ICSD-2, ICSD-3 and ICD-11 criteria.

4.2.3.2 Rosters

Working-hour characteristics were obtained from the participants' rosters. Working hours were double-checked in the sleep diary data.

4.2.3.3 Three-week field measurements

Actigraphy and sleep diary monitoring continued for three weeks. For the purpose of this study, data on days off (after a day off; a day on which a night shift ended was not regarded as a day off), morning shifts, evening shifts (not followed by a morning shift), and night shifts were examined as presented in Figure 3.

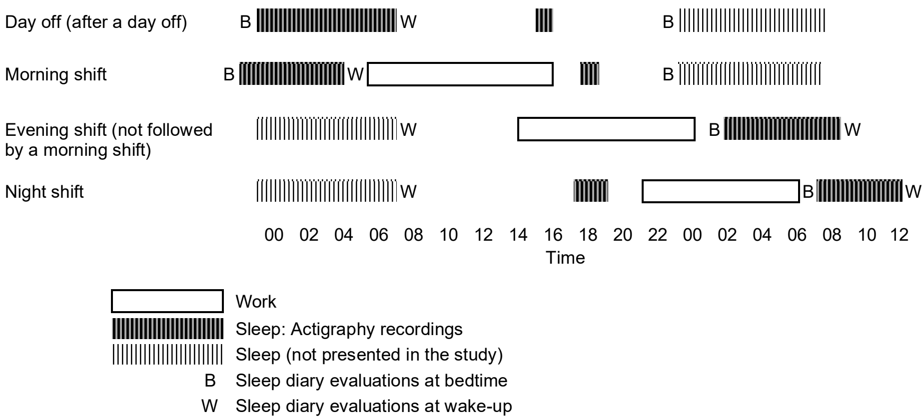

Figure 3 Schematic timing of actigraphy recordings (sleep latency, sleep efficiency, and 24-hour TST) and sleep diary evaluations at bedtime (B; shift start and end times, greatest KSS sleepiness of the day, start and end time of naps, bedtime stress, and bedtime) and at wake-up (W; sleep latency of main sleep, sleep quality, number of awakenings, TST of main sleep, and wake-up time) in Study III.

Actigraphy

Actigraphy monitoring was used to objectively measure sleep–wake rhythm. The ground staff members wore an actigraph Actiwatch AW7 (Cambridge Neurotechnology Ltd, Cambs, UK) on their non-dominant wrist. Actiwatch Activity and Sleep Analysis 7 software (Cambridge Neurotechnology Ltd, Cambs, UK) was used to build variables including TST, sleep latency (< 30 minutes indicated normal sleep latency) (Sateia et al. 2017), and sleep efficiency (< 85% sleep efficiency indicated disturbed sleep) (Astill et al. 2013) from one-minute epochs. I calculated 24-hour TST by adding the TST of main sleep and naps together.

Sleep diary

Sleep diary monitoring was used to subjectively observe the sleep-wake rhythm. The participants filled in a sleep diary twice a day. At bedtime, they evaluated shift start and end times, the greatest KSS sleepiness of each day (Ingre et al. 2004), bedtime stress (nine-point scale from 1 = 'very calm and relaxed' to 9 = 'extremely stressed and tense'), and bedtime. At awakening, they evaluated wake-up time, the sleep latency of main sleep, the quality of sleep (five-point scale from 1 = 'good' to 5 = 'poor'), and the number of awakenings. I calculated 24-hour TST by adding the TST of main sleep and naps together. Sleep debt was calculated by subtracting sleep diary-based 24-hour TST from subjective sleep need (Hublin et al. 2001).

4.2.3.4 Predetermined days of PVT, KSS, and EEG measurements

During the three-week field monitoring, the ground staff members took PVTs, reported the last five minutes' KSS ratings, and carried out EEG-based sleep recording on six predetermined days in connection with two days off, two morning shifts (starting by 06:00), and two night shifts. (Figure 4)

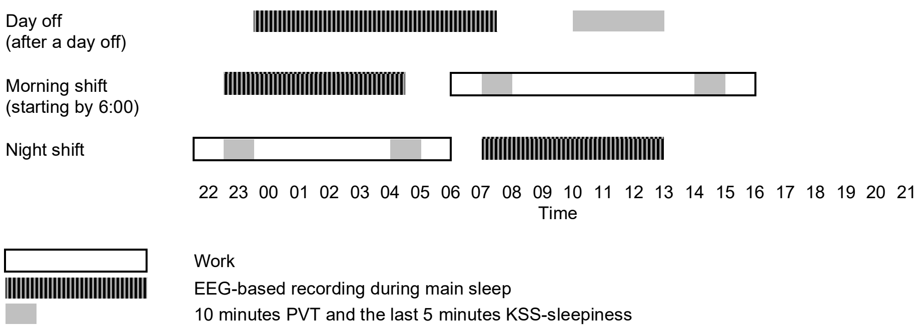

Figure 4 Schematic timing of PVT, the last five minutes' KSS sleepiness, and EEG-based sleep measurements in relation to predetermined days off, morning shifts, and night shifts in Study III.

PVT

Vigilant attention was measured using a 10-minute reaction time test, a PVT, installed on mobile phones (HP ipaq 514, Hewlett-Packard Company, Palo Alto, CA, USA) (Karhula et al. 2013). On days off, the ground staff members took PVTs between 10:00 and 13:00. During morning and night shifts, the

PVTs were taken 1–2 hours after the start and 1–2 hours before the end of the shifts (Figure 4). To avoid disturbance, the ground staff members were asked to complete the measurements in a quiet place. To minimise the learning effect, they were instructed to practise the PVT three times before the first predetermined measurement (Dinges et al. 1997). Mean reaction time (ms) and the number of > 500 ms reaction times (lapses) were included in the study.

KSS sleepiness

Before each PVT during the predetermined six days, ground staff members evaluated their last five minutes' KSS sleepiness on the HP ipaq 514 mobile phones (Figure 4). As mentioned above (See 'Sleep diary' paragraph above), they also assessed their greatest sleepiness on each day during the three-week field study in the sleep diary.

EEG-based sleep recordings

A consumer-friendly wireless single-channel system, Zeo Sleep Manager (Zeo, Inc., Newton, MA, USA), was used to record sleep EEG from the forehead. The system has been validated against PSG (Shambroom et al. 2012; Griessenberger et al. 2013). The Zeo Sleep Manager scores epochs of 30 s in four stages: light sleep, SWS, REM sleep, and wakefulness – and produces acceptable sleep scoring for the first three. When Griessenberger et al. (2013) compared the Zeo Sleep Manager with semiautomatic Somnolyzer 24 × 7 sleep scoring software using polysomnographic data, the Zeo Sleep Manager detected 80% (Cohen's kappa, κ 0.79) of the study standard light sleep epochs, 74% (κ 0.79) of the REM sleep epochs, 62% (κ 0.82) of the SWS epochs, and 41% (κ 0.32) of the wakefulness epochs. Overall, the system has shown moderate agreement (73%–76%, κ 0.56–0.62) in comparison to PSG (Shambroom et al. 2012; Griessenberger et al. 2013).

The ground staff members recorded their sleep at home during the same six predetermined days as they completed the PVTs: after a day off, before a morning shift, and after a night shift (Figure 4). To get used to the device, they were instructed to sleep one night wearing the headband of the device before the first recording. They were also asked not to consume alcohol on the day before each sleep EEG recording. The EEG-based variables included the TST of main sleep, REM sleep, light sleep, and SWS.

4.2.4 STATISTICAL ANALYSES

Analyses were carried out using IBM SPSS Statistics 20.0 (Study III). P-values under 0.05 indicate statistical significance. Although multiple analyses were run, the significance level was not set lower, as the number of participants was limited. Power calculations were not made because the number of ground staff members was expected to be high enough. Effect sizes were also not calculated.

4.2.4.1 Non-repeated measurements

Depending on the scale and distribution of each online questionnaire variable, the groups were compared using the Fisher's exact test, the Mann–Whitney U test, or the independent samples t test.

4.2.4.2 Repeated measurements

To consider the individual composition of work schedules, the linear mixed model (LMM) analysis, with group and age as the main effects, was used to compare the normally distributed continuous variables of the groups. Chronotype was also used instead of age as the main effect. However, the results for the LMM analyses adjusted for chronotype are not presented, as they gave similar results to those of the analyses adjusted for age. If possible, the variables that did not meet the model assumptions were transformed as follows:

$\sqrt{x}$	EEG-based TST of main sleep (day off), REM sleep (night shift), and SWS (day off and night shift)
$\log_{10} x$	SWS (morning shift)
$\sqrt{x_{max} + 1 - x}$	Light sleep (morning shift) and sleep efficiency (day off, evening shift, and night shift)
$\log_{10}(x_{max} + 1 - x)$	Sleep efficiency (morning shift)

If a variable could not be transformed to meet the model assumptions, the Mann–Whitney U test was used to compare the groups. Apart from the LMM analyses results, the statistics of repeated measures were calculated from each ground staff member's mean values.

5 RESULTS

5.1 STUDY I

5.1.1 DESCRIPTIVE CHARACTERISTICS

In Study I, the mean (standard deviation, SD) age of the participants (n = 4 814) was 42.8 (11.5) years, 91% of them were women, and 88% were healthcare professionals, 9% maintenance workers, and 3% assistants or office workers. The most common job titles were registered nurse (53%), practical nurse (14%), midwife (5%), and hospital cleaner (4%). Tables 4–5 show the characteristics of the shift workers with ICSD-3-based SWD in relation to a cut-off of days with SWD symptoms. In addition, five permanent night workers screened positive for ICSD-3-based SWD. Their mean (SD) age was 47.2 (6.6) years, three of them were women, all of them were late chronotypes and experienced fatigue on ≥ 2 days off per week, none had sleep apnoea, one had RLS, and one suffered from depression.

Table 4 *Characteristics of shift workers without night shifts who screened positive for ICSD-3-based SWD, in relation to cut-offs of ≥ 1 (n = 67), ≥ 3 (n = 50), ≥ 5 (n = 32), and ≥ 7 (n = 11) days with SWD symptoms (and non-day shifts) per month (Study I).*

	Cut-off			
	≥ 1	**≥ 3**	**≥ 5**	**≥ 7**
Age, mean (SD) years	44.5 (11.1)	44.6 (11.4)	43.3 (12.0)	40.1 (13.2)
Women, % (n)	97 (65)	96 (48)	97 (31)	100 (11)
Late chronotype, % (n)	60 (40)	54 (27)	59 (19)	64 (7)
Sleep apnoea, % (n)	3 (2)	4 (2)	3 (1)	0 (0)
Restless legs syndrome, % (n)	9 (6)	12 (6)	19 (6)	18 (2)
Depression, % (n)	10 (7)	12 (6)	13 (4)	18 (2)
Fatigue on ≥ 2 days off per week, % (n)	39 (26)	40 (20)	41 (13)	55 (6)

Table 5 *Characteristics of shift workers with night shifts who screened positive for ICSD-3-based SWD, in relation to cut-offs of ≥ 1 (n = 276), ≥ 3 (n = 167), ≥ 5 (n = 96), and ≥ 7 (n = 53) days with SWD symptoms (and non-day shifts) per month (Study I).*

	Cut-off			
	≥ 1	**≥ 3**	**≥ 5**	**≥ 7**
Age, mean (SD) years	40.1 (10.6)	39.4 (10.7)	40.3 (11.1)	41.4 (10.9)
Women, % (n)	87 (240)	86 (143)	81 (78)	77 (41)
Late chronotype, % (n)	67 (184)	72 (120)	69 (66)	70 (37)
Sleep apnoea, % (n)	1 (4)	1 (1)	1 (1)	2 (1)
Restless legs syndrome, % (n)	6 (16)	7 (11)	7 (7)	11 (6)
Depression, % (n)	10 (27)	9 (15)	9 (9)	8 (4)
Fatigue on ≥ 2 days off per week, % (n)	44 (121)	49 (82)	51 (49)	55 (29)

5.1.2 PREVALENCE OF SWD

Table 6 presents the prevalence rates of ICSD-2-based SWD and ICSD-3-based SWD among shift workers without and with night shifts. Based on the 95% CI-values, the prevalence rates of ICSD-3-based SWD were lower than those of ICSD-2-based SWD among both shift workers without night shifts and shift workers with night shifts in relation to all the used cut-offs of non-day shifts. Among permanent night workers, the difference between the prevalence of ICSD-3-based SWD (6%, 95% CI 1%–11%) and ICSD-2-based SWD (17%, 95% CI 9%–25%) was not significant. According to the Pearson chi-squared tests, the prevalence of SWD was significantly lower among the shift workers without night shifts than among the shift workers with night shifts in relation to the cut-offs of ≥ 1 and ≥ 3 non-day shifts per month, but not in relation to the higher cut-offs, regardless of the ICSD criteria used (Table 6).

Table 6 *Prevalence of SWD among shift workers without and with night shifts in relation to cut-offs of ≥ 1, ≥ 3, ≥ 5, and ≥ 7 non-day shifts (and days with SWD symptoms) a month by shift work schedule and ICSD criteria (Study I).*

	ICSD-2								**ICSD-3**							
	Shift work without night shifts			**Shift work with night shifts**					**Shift work without night shifts**			**Shift work with night shifts**				
	%	**(95% CI)**	**(n)**	**%**	**(95% CI)**	**(n)**	**χ^2**	**p**	**%**	**(95% CI)**	**(n)**	**%**	**(95% CI)**	**(n)**	**χ^2**	**p**
≥ 1	9	(8–11)	(167)	34	(32–35)	(980)	362.4	<0.001	4	(3–5)	(67)	10	(8–11)	(276)	55.3	<0.001
≥ 3	9	(7–10)	(127)	18	(17–20)	(529)	70.5	<0.001	3	(3–4)	(50)	6	(5–7)	(167)	11.4	<0.001
≥ 5	8	(6–9)	(75)	9	(8–10)	(230)	0.6	0.428	3	(2–4)	(32)	4	(3–4)	(96)	0.2	0.691
≥ 7	7	(5–10)	(31)	6	(5–7)	(114)	1.5	0.224	3	(1–4)	(11)	3	(2–3)	(53)	0.0	0.914

The exclusion of shift workers with sleep apnoea, RLS, and/or depression only marginally changed SWD prevalence. For instance, when the cut-off of ≥ 3 non-day shifts was used, the prevalence of ICSD-2-based SWD became 0.1% greater and the prevalence of ICSD-3-based SWD became 0.2% smaller among shift workers with night shifts. Among shift workers without night shifts, the corresponding prevalence rates became 0.3% and 0.4% smaller, respectively.

5.1.3 DAYS WITH ICSD-3-BASED SWD SYMPTOMS PER MONTH

Figure 5 shows that 38% of the shift workers with night shifts who reported ICSD-3-based symptoms of SWD had them on < 3 days per month. The percentage was 45 among the shift workers without night shifts. Among the shift workers with night shifts, the mode of days per month with SWD symptoms was two. Among the shift workers without night shifts, the mode was < 1. However, it should be noted that the shift workers who reported symptoms of SWD in the survey, but had them less often than once per month, were considered non-SWD cases, as the occurrence of SWD symptoms was especially infrequent.

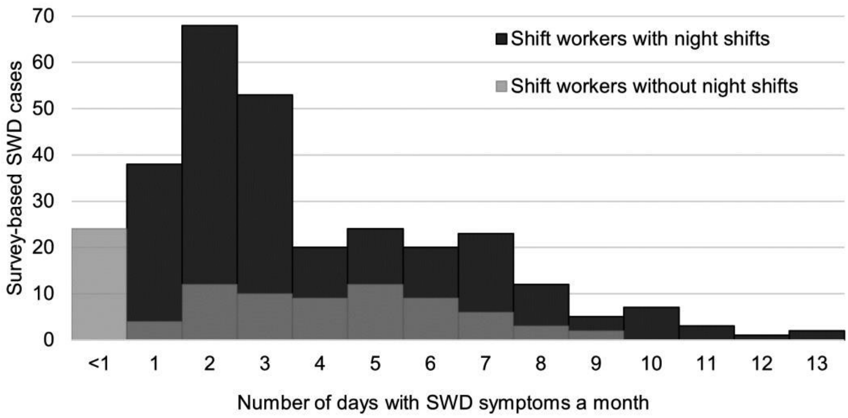

Figure 5 Survey-based SWD (ICSD-3) cases in relation to number of days with ICSD-3-based SWD symptoms per month among shift workers with (n = 276) and without (n = 91) night shifts (Study I).

5.1.4 FATIGUE ON WEEKLY DAYS OFF

I compared the prevalence of fatigue on ≥ 2 days off per week among those who had a higher number of days with ICSD-3-based SWD symptoms per month with those who had a lower number of such days (< 3 and ≥ 3, < 5 and ≥ 5, and < 7 and ≥ 7 days with symptoms). This same comparison was made both among shift workers without night shifts (n = 17 and 50, 35 and 32, and 56 and 11, respectively) and among shift workers with night shifts (n = 109 and 167, 180 and 96, and 223 and 53, respectively). Based on Fisher's exact test, fatigue on ≥ 2 days off per week was significantly more prevalent among shift workers with night shifts who had ≥ 3 days with SWD symptoms (49%) than among those who had < 3 days with SWD symptoms (36%, $p = 0.035$). The other comparisons showed no statistical differences.

5.2 STUDY II

5.2.1 DESCRIPTIVE CHARACTERISTICS

The study population of Study II consisted of 2 900 shift workers with night shifts (with ≥ 3 non-day shifts per month). The mean (SD) age of the participants was 40.5 (11.3) years, mean (SD) shift work experience was 13.5 (9.9) years, 89% (n = 2 575) of them were women, 66% (n = 1 900) were late chronotypes, 47% (n = 1 213) lived with children, 1% (n = 31) had sleep apnoea, 3% (n = 86) had RLS, and 9% (n = 247) suffered from depression. As presented in Study I, 18% (n = 529) screened positive for ICSD-2-based SWD. In addition, 8% (n = 244) were classed as positive for SWD-Es, 6% (n = 183) for SWD-IEs, and 4% (n = 102) for SWD-I. Of the study population, 95% were healthcare professionals. The most common job titles included registered nurse (63%, n = 1 826), practical nurse (13%, n = 381), midwife (6%, n = 179), and psychiatric nurse (4%, n = 116).

5.2.2 INSOMNIA AND EXCESSIVE SLEEPINESS ON DAYS OFF AND SLEEP LENGTH

Table 7 shows the prevalence rates of insomnia on weekly days off, excessive sleepiness on weekly days off, and subjective 24-hour sleep length among shift workers without SWD, shift workers with any SWD, and shift workers with the three subtypes of SWD in Study II.

Table 7 *Prevalence of insomnia on weekly days off, excessive sleepiness on weekly days off, and subjective 24-hour sleep length among participants without SWD (n = 2 371), with SWD (n = 529), and with different subtypes of SWD (SWD-Es, n = 244; SWD-IEs, n = 183; SWD-I, n = 102) (Study II).*

	Non-SWD	SWD			
		Any	Subtypes		
			SWD-Es	SWD-IEs	SWD-I
	% (n)	% (n)	% (n)	% (n)	% (n)
Insomnia on weekly days off	7 (154)	3 (17)	4 (9)	3 (5)	3 (3)
Excessive sleepiness on weekly days off	12 (281)	16 (82)	14 (33)	15 (28)	21 (21)
Subjective 24-hour sleep					
≤ 6.5 hours	26 (616)	27 (140)	21 (52)	28 (51)	36 (37)
7–7.5 hours	44 (1045)	44 (235)	45 (109)	43 (79)	46 (47)
≥ 8 hours	29 (692)	29 (153)	34 (83)	28 (52)	18 (18)

According to the logistic regression analyses (Table 8), SWD was associated with decreased odds of insomnia on weekly days off and increased odds of excessive sleepiness on weekly days off. SWD was not associated with subjective 24-hour sleep length.

Table 8 *Crude and adjusted logistic regression analyses with insomnia on weekly days off, excessive sleepiness on weekly days off, and subjective 24-hour sleep as dependent variables (Study II).*

	Insomnia on weekly days off	Excessive sleepiness on weekly days off	Subjective 24-hour sleep length (reference: ≥ 8 hours)	
			≤ 6.5 hours	7–7.5 hours
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
CRUDE				
SWD	0.48 (0.29–0.80)	1.36 (1.04–1.77)	1.03 (0.80–1.33)	1.02 (0.81–1.24)
ADJUSTED [a]				
SWD	0.53 (0.31–0.91)	1.42 (1.07–1.88)	1.06 (0.81–1.40)	1.06 (0.84–1.35)

[a] Adjusted for age, sex, living with children, sleep apnoea, RLS, and depression.

According to the logistic regression analyses (Table 9), none of the SWD subtypes were significantly associated with insomnia on weekly days off. SWD-I was significantly associated with increased odds of excessive sleepiness on weekly days off in both the crude and adjusted analyses. In addition, compared to subjective sleep of ≥ 8-hours (per 24-hours), SWD-I was significantly associated with both sleep of ≤ 6.5 hours (in the crude and adjusted analyses) and sleep of 7–7.5 hours (only in the adjusted analysis). SWD-Es or SWD-IEs were not significantly associated with either excessive sleepiness on weekly days off or subjective 24-hour sleep length.

Table 9 *Crude and adjusted logistic regression analyses with insomnia on weekly days off, excessive sleepiness on weekly days off, and subjective 24-hour sleep as dependent variables (Study II).*

	Insomnia on weekly days off	Excessive sleepiness on weekly days off	Subjective 24-hour sleep length (reference: ≥ 8 hours)	
			≤ 6.5 hours	7–7.5 hours
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
CRUDE				
SWD-Es	0.55 (0.28–1.09)	1.16 (0.79–1.71)	0.70 (0.49–1.01)	0.87 (0.64–1.18)
SWD-IEs	0.41 (0.17–1.00)	1.33 (0.88–2.03)	1.10 (0.74–1.65)	1.01 (0.70–1.45)
SWD-I	0.43 (0.14–1.38)	1.94 (1.17–3.14)	2.31 (1.30–4.10)	1.73 (0.10–3.00)
ADJUSTED [a]				
SWD-Es	0.60 (0.29–1.26)	1.16 (0.77–1.76)	0.79 (0.53–1.17)	0.92 (0.67–1.27)
SWD-IEs	0.44 (0.18–1.10)	1.39 (0.89–2.16)	1.06 (0.70–1.63)	1.00 (0.69–1.46)
SWD-I	0.54 (0.17–1.75)	2.25 (1.31–3.87)	2.39 (1.24–4.59)	1.96 (1.06–3.63)

[a] Adjusted for age, sex, living with children, sleep apnoea, RLS, and depression.

5.3 STUDY III

5.3.1 DESCRIPTIVE CHARACTERISTICS

Table 10 shows the characteristics of the SWD (n = 22) and reference (n = 9) groups. The SWD group was younger (mean difference - 6.6 years, 95% CI - 3.1–- 0.2), had lower flexibility of sleeping habits (mean difference - 6.2, 95% CI - 10.6–- 1.9), and consumed less caffeine (U 50.0, p = 0.03) than the reference group. No significant differences were found when sex, chronotype, length of shift work experience, frequency of physical exercise, consumption of alcohol, smoking, and having OSA (treated) were compared. The number of shift types, consecutive shifts (per shift type), consecutive days off, or shift start and end times (per shift type) of the groups did not significantly differ (p-values ≥ 0.19, data not shown).

Table 10 *Characteristics of SWD (n = 22) and reference (n = 9) groups (Study III).*

	SWD	Reference	p
Age, mean (SD) years	41 (8)	48 (7)	0.04 [a]
Men, % (n)	77 (17)	78 (7)	1.00 [b]
Early chronotype, % (n)	36 (8)	56 (5)	0.43 [b]
Flexibility of sleeping habits, mean (SD)	26 (6)	33 (4)	< 0.01 [a]
Shift work experience, mean (SD) years	17 (8)	23 (13)	0.20 [a]
Physical exercise, % (n)	50 (11)	22 (2)	0.29 [b]
Consumption of caffeinated drinks per day, median (IQR)	4 (5)	5 (2)	0.03 [c]
Alcohol consumption ≥ 2 times per month, % (n)	50 (11)	67 (6)	0.46 [b]
Smoker, % (n)	14 (3)	11 (1)	1.00 [b]
Treated sleep apnoea, % (n)	5 (1)	11 (1)	0.50 [b]

[a] Independent samples t-test, [b] Fisher's Exact Test, [c] Mann-Whitney U-test

5.3.2 QUANTITY OF SLEEP

According to the Mann-Whitney U test, the SWD group reported having a longer sleep need (median 8:00, interquartile range, IQR 2:00) than the reference group (median 7:00, IQR 2:00, U 50.0; p = 0.03). In addition, according to the results of the LMM analyses shown in Table 11, the SWD group had significantly more sleep debt on morning shift days (p < 0.01) and less compensatory sleep on days off (p = 0.01) than the reference group. Further, the SWD group had significantly shorter subjective 24-hour TST in connection with morning shift days than the reference group (p = 0.04). The objective TST of the groups did not significantly differ.

Table 11 *Quantity of sleep in SWD and reference groups (Study III).*

	SWD group		Reference group			Group	
	Mean (SD)	**(n)**	**Mean (SD)**	**(n)**	**df**	**F**	**p [a]**
SLEEP DEBT [b]							
Days off	-0:05 (1:08)	(22)	-1:32 (1:36)	(8)	25.567	7.44	0.01
Before morning shifts	1:58 (0:50)	(22)	0:23 (1:49)	(8)	26.834	11.13	< 0.01
After evening shifts	0:54 (1:19)	(22)	-0:09 (1:20)	(9)			0.07
After night shifts	1:36 (1:22)	(18)	0:51 (1:08)	(8)			0.14
24-HOUR TST, SLEEP DIARY [b]							
Days off	7:58 (1:02)	(22)	8:17 (0:48)	(8)			0.49
Before morning shifts	5:55 (0:46)	(22)	6:30 (0:37)	(8)	22.258	4.94	0.04
After evening shifts	6:59 (1:10)	(22)	7:03 (1:08)	(9)			0.90
After night shifts	6:16 (1:15)	(18)	5:54 (1:20)	(8)			0.49
24-HOUR TST, ACTIGRAPHY [b]							
Days off	7:19 (0:54)	(22)	7:58 (0:55)	(9)			0.17
Before morning shifts	5:37 (0:49)	(22)	6:08 (0:43)	(8)			0.20
After evening shifts	6:17 (0:59)	(22)	6:45 (0:59)	(9)			0.31
After night shifts	5:48 (1:07)	(18)	5:46 (0:59)	(8)			0.98
TST OF MAIN SLEEP, EEG-BASED RECORDINGS [b]							
Days off	7:05 (1:23)	(22)	8:02 (0:46)	(9)			0.10
Before morning shifts	5:34 (0:58)	(22)	5:53 (0:41)	(8)			0.67
After night shifts	5:02 (1:29)	(17)	4:55 (1:36)	(8)			0.64

[a] LMM with group and age as main effects [b] h:mm

According to the LMM analyses of the sleep stages, the SWD group had less light sleep on days off (mean 3:51, SD 1:05) than the reference group (mean 4:54, SD 1:07; Group: $F_{28.844} = 6.02$; p = 0.02). No other significant differences were found between the groups in terms of sleep stages (light sleep: p ≥ 0.14, REM sleep: p ≥ 0.27, SWS: p ≥ 0.45).

5.3.3 QUALITY OF SLEEP

Table 12 shows the results of the Mann-Whitney U tests in terms of subjective and objective quality of sleep. Sleep diary reports showed that, compared to the reference group, the SWD group had significantly poorer self-estimated sleep quality across all days (p-values < 0.01) and significantly longer subjective sleep latency in connection with days off (p = 0.03), morning shifts (p < 0.01), and night shifts (p < 0.01). Likewise, actigraphy recordings indicated significantly longer objective sleep latency in relation to morning (p = 0.03), evening (p = 0.03), and night (p = 0.04) shifts. All the sleep latency medians were < 30 minutes, indicating a rather good level of sleep latency (Sateia et al. 2017). The median number of awakenings during a sleep period in the SWD and reference groups did not significantly differ (p-values ≥ 0.19, data not shown).

Table 12 *Objective and subjective sleep quality in SWD and reference group (Study III).*

	SWD group		Reference group			
	Median (IQR)	**(n)**	**Median (IQR)**	**(n)**	**U**	**p[a]**
QUALITY OF SLEEP, SLEEP DIARY [b]						
Days off	2.7 (0.9)	(22)	1.3 (0.4)	(8)	17.5	< 0.001
Before morning shifts	3.0 (0.9)	(22)	1.6 (0.8)	(8)	13.5	< 0.001
After evening shifts	2.3 (1.0)	(22)	1.0 (0.4)	(9)	21.5	< 0.001
After night shifts	2.5 (1.4)	(18)	1.5 (0.9)	(8)	18.0	< 0.01
SLEEP LATENCY, SLEEP DIARY [c]						
Days off	0:16 (0:08)	(22)	0:08 (0:11)	(8)	49.0	0.03
Before morning shifts	0:20 (0:34)	(22)	0:09 (0:10)	(8)	31.0	< 0.01
After evening shifts	0:12 (0:08)	(22)	0:08 (0:11)	(9)	59.5	0.08
After night shifts	0:11 (0:08)	(18)	0:05 (0:04)	(8)	21.5	< 0.01
SLEEP LATENCY, ACTIGRAPHY [c]						
Days off	0:08 (0:07)	(22)	0:04 (0:05)	(9)	56.5	0.06
Before morning shifts	0:06 (0:08)	(22)	0:03 (0:06)	(8)	42.0	0.03
After evening shifts	0:08 (0:12)	(22)	0:03 (0:06)	(9)	48.0	0.03
After night shifts	0:03 (0:04)	(18)	0:02 (0:03)	(8)	35.0	0.04

[a] Mann-Whitney U-test, [b] 1 = good, 5 = poor, [c] h:mm

Further, according to the LMM analyses, the actigraphy-based sleep efficiency was significantly lower in the SWD group than in the reference group in connection with days off (p < 0.01), morning shifts (p < 0.01), and evening shifts (p < 0.01). All the sleep efficiency means (Table 13) were > 85%, which is a satisfactory level (Astill et al. 2013).

Table 13 *Sleep efficiency (%) based on actigraphy recordings in SWD and reference groups (Study III).*

	SWD group		Reference group		Group		
	Mean (SD)	**(n)**	**Mean (SD)**	**(n)**	**df**	**F**	**p[a]**
Days off	89 (5)	(22)	94 (2)	(9)	29.041	11.91	< 0.01
Before morning shifts	87 (6)	(22)	93 (4)	(8)	27.304	11.84	< 0.01
After evening shifts	89 (4)	(22)	94 (3)	(9)	25.924	13.66	< 0.01
After night shifts	90 (4)	(18)	93 (3)	(8)	22.373	3.73	0.07

[a] LMM with group and age as main effects

Besides poorer subjective and objective quality of sleep, the results of the Mann-Whitney U tests indicated higher self-evaluations on the bedtime stress scale in the SWD group than in the reference group in connection with days off ($p < 0.01$), morning shifts ($p < 0.01$), evening shifts ($p < 0.01$), and night shifts ($p = 0.04$, Table 14).

Table 14 *Bedtime stress based on sleep diary evaluations in SWD and reference groups (Study III).*

	SWD group		Reference group			
	Median (IQR)	**(n)**	**Median (IQR)**	**(n)**	**U**	**p[a]**
Days off [b]	2 (1)	(22)	1 (1)	(8)	26.0	< 0.01
Before morning shifts [b]	3 (3)	(22)	1 (1)	(8)	24.0	< 0.01
After evening shifts [b]	3 (2)	(22)	1 (2)	(9)	39.5	< 0.01
After night shifts [b]	3 (2)	(18)	2 (3)	(8)	35.5	0.04

[a] Mann-Whitney U-test, [b] 1 = very calm and relaxed, 9 = extremely stressed and tense

5.3.4 SUBJECTIVE SLEEPINESS AND OBJECTIVE ALERTNESS

Figure 6 presents the greatest KSS sleepiness of each day in the SWD and reference groups. According to the Mann–Whitney U tests, the greatest KSS sleepiness was significantly greater in the SWD group on morning shift ($U = 30.5$, $p < 0.01$) and evening shift ($U = 52.5$, $p = 0.04$) days than in the reference group. The difference was not significant on days off ($U = 47.0$, $p = 0.09$) or on night shift days ($U = 41.5$, $p = 0.09$).

Similarly, Figure 7 presents the last five minutes' KSS sleepiness on days off and during morning and night shifts. According to the Mann–Whitney U tests, the last five minutes' KSS sleepiness was significantly greater in the SWD group at the beginning ($U = 17.0$, $p < 0.001$) and at the end ($U = 36.0$, $p = 0.01$) of morning shifts, as well as at the end of night shifts ($U = 30.0$, $p = 0.02$) than in the reference group. The difference was not significant between 10:00 and 13:00 hours on days off ($U = 55.0$, $p = 0.05$) or at the beginning of night shifts ($U = 39.0$, $p = 0.07$).

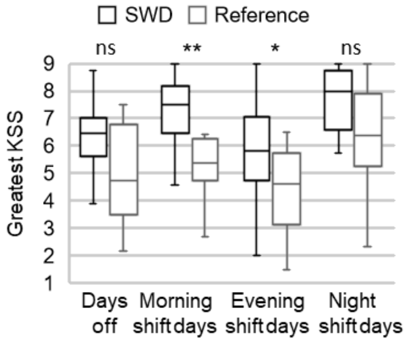

Figure 6 Maximum (unpublished), third quartile, median, first quartile, and minimum (unpublished) of the greatest KSS sleepiness of each day. ns p ≥ 0.05, * p < 0.05, and ** p < 0.01 (Study III).

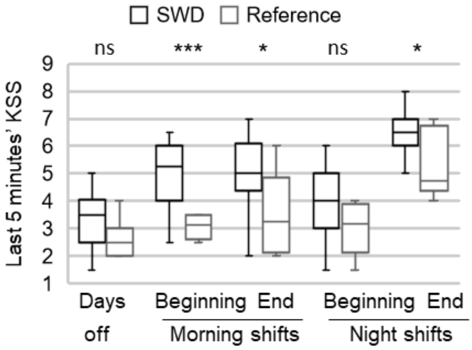

Figure 7 Maximum (unpublished), third quartile, median, first quartile, and minimum (unpublished) of last five minutes' KSS at beginning of shifts, at end of shifts, and on days off (between 10:00–13:00 hours). ns p ≥ 0.05, *p < 0.05, and ***p < 0.001 (Study III).

According to the Mann–Whitney U test, the SWD group had significantly more lapses (> 500 ms reaction times) in PVT at the beginning of night shifts than the reference group (p = 0.04, Table 15). The median reaction times of the SWD and reference groups did not significantly differ (p-values ≥ 0.18, data not shown).

Table 15 *Number of lapses in PVT in SWD and reference groups (Study III).*

	SWD group		Reference group			
	Median (IQR)	**(n)**	**Median (IQR)**	**(n)**	**U**	**p[a]**
Days off [b]	0.0 (1.0)	(21)	0.5 (1.3)	(9)		0.77
Beginning of morning shifts	0.7 (1.3)	(21)	0.5 (0.9)	(8)		0.27
End of morning shifts	0.5 (1.3)	(21)	0.1 (2.0)	(8)		0.19
Beginning of night shifts	0.5 (0.6)	(18)	0.0 (0.0)	(8)	39.0	0.04
End of night shifts	1.0 (4.4)	(18)	0.8 (3.1)	(8)		0.61

[a] Mann-Whitney U-test, [b] 10:00–13:00 hours

6 DISCUSSION

This thesis examined 1) the prevalence of SWD based on both ICSD-2 and ICSD-3 criteria among hospital employees with different shift arrangements, 2) the manifestation of SWD in relation to naturalistic work shifts among airport ground staff members, and 3) recovery from SWD on days off among hospital employees and ground staff. The hospital employee data of Studies I and II comprised a representative epidemiological survey linked to registry data on working hours. The ground staff data of Study III comprised questionnaires and field data. SWD was defined as shift work schedule-related symptoms that decreased during a longer holiday.

Based on the epidemiological findings, estimates of SWD prevalence appear to be lower when ICSD-3 criteria are used than when ISCD-2 criteria are used. In addition, many employees who reported primary symptoms of SWD, only had them sporadically. Field findings suggest that although SWD manifests in relation to night shifts (e.g., as greater KSS sleepiness and greater number of lapses in PVT), morning shifts (e.g., greater KSS sleepiness, shorter subjective TST, and more sleep debt) and quality of sleep in particular distinguish shift workers with SWD from those without SWD. Further, SWD was related to poorer recovery on days off in both the epidemiological and field studies.

6.1 PREVALENCE OF SWD

Using the ICSD-3 criteria resulted in lower estimates of SWD prevalence than when the ICSD-2 criteria were used among shift workers both with and without night shifts in Study I. The differences between the prevalence estimates were particularly notable among shift workers with night shifts when employees with fewer non-day shifts (1–4 per month) were also included. It should be noted that only one non-day shift a month does not technically meet the ICSD's requirement of a recurring overlap of work and conventional time for sleep. Thus, a cut-off of ≥ 1 non-day shift a month served as the reference level in Study I. The above finding suggests that the proportion of false positives is high among shift workers with infrequent shifts related to insomnia and/or excessive sleepiness, especially when using the ICSD-2 criteria for SWD. This was also indicated as a greater decrease in the ICSD-2-based estimate of SWD prevalence than in the ICSD-3-based estimate among shift workers with night shifts when those with the fewest non-day shifts were excluded.

Regardless of the ICSD criteria, shift workers with night shifts had higher estimates of SWD prevalence than shift workers without night shifts when the analyses included hospital employees with fewer non-day shifts (1–4 per month, Study I). A similar trend was described (but not statistically tested) in the ICSD-2-based estimates of SWD prevalence among nurses in Norway (Flo et al. 2012). In line with this, self-reported night shifts (Waage et al. 2014) and quick returns (Flo et al. 2014) increased the risk of ICSD-2-based SWD in the cohort of nurses.

Studies typically select shift workers on the basis of their self-reported shift schedules, as in the above studies of nurses in Norway. The number of self-reported shifts, for example, ≥ 1 (Rajaratnam et al. 2011) and ≥ 5 (Czeisler et al. 2009) night shifts a month, has also been used as an inclusion cut-off for shift workers. In this thesis (Study I), the estimates of SWD prevalence among employees with and employees without night shifts did not differ if they had ≥ 5 non-day shifts a month. Thus, the timing of non-day shifts appears not to considerably affect SWD prevalence if the symptoms of SWD occur frequently. Therefore, in addition to night shifts, it could be relevant to consider other non-day shifts, for example, evening and morning shifts, in cut-offs of future SWD studies.

Many shift workers evaluated having SWD symptoms in relation to non-day shifts which, based on the objective data, recurred rarely (Study I). This probably caused the decrease in the estimates of SWD prevalence when shift workers with fewer non-day shifts were excluded. Frequent non-day shifts hardly produce less SWD symptoms than a small amount of non-day shifts (Waage et al. 2014), which could not be tested in a cross-sectional setting of Study I. Thus, the higher SWD prevalence — when employees with infrequent non-day shifts were also included — possibly resulted from the healthy worker effect (Knutsson and Åkerstedt 1992), based on which individuals who cope with circadian disruption or sleep loss would be over-represented in more demanding shift schedules. Likewise, individuals who cannot cope with demanding schedules and may thus report SWD symptoms may have possibly transferred to schedules with infrequent non-day shifts, thus increasing the SWD prevalence estimate in these schedules.

SWD prevalence studies typically incorporate a connection between the symptoms of SWD and shift work in their SWD screening instrument (Waage et al. 2009; Rajaratnam et al. 2011; Flo et al. 2012; Asaoka et al. 2013; Barger et al. 2015; Taniyama et al. 2015; Booker et al. 2020b; Chen et al. 2020). However, as far as I am aware, SWD prevalence studies have not used minimum cut-offs for the occurrence of shift work-related insomnia and excessive sleepiness when defining SWD (nor do the coding manuals specify the cut-off). Although a few studies have set the cut-off of overall insomnia (not specifically related to shift work) to *at least sometimes* (Drake et al. 2004), to *at least a few times a week* (Swanson et al. 2011), and to *more than three times a week* (Chen et al. 2020) in their SWD screening instruments, these cut-offs have not been applied to excessive sleepiness. In fact, the excessive sleepiness component of SWD is often defined as excessive daytime sleepiness on a general level (Drake et al. 2004; Gumenyuk et al. 2010; Swanson et al. 2011; Gumenyuk et al. 2012; Gumenyuk et al. 2014; Belcher et al. 2015; Gumenyuk et al. 2015; Kalmbach et al. 2015; Kerkhof 2018; Chen et al. 2020), although the SWD symptoms should stem from shift working hours (Wright et al. 2013; AASM 2014).

Therefore, a preliminary sub-study of this thesis (as part of Study I) sought a minimum cut-off for the occurrence of ICSD-3-based SWD symptoms using fatigue on weekly days off as an indicator of insufficient recovery from shift work. This is because Härmä et al. (2018) have shown that a change in the occurrence of non-day shifts is associated with a parallel change in the occurrence of fatigue on days off among hospital employees, and because quick returns have shown to increase the risk of pathological fatigue among nurses (Flo et al. 2014). The prevalence of insufficient recovery appeared to increase among the hospital employees with ICSD-3-based SWD in this thesis as the occurrence of days with SWD symptoms increased. Among the shift workers with night shifts, insufficient recovery was significantly more common if ICSD-3-based SWD symptoms occurred on ≥ 3 compared to < 3 days a month. This finding implies that three days with SWD symptoms a month may be used as a minimum cut-off for ICSD-3-based SWD cases in epidemiological studies.

The prevalence of ICSD-2-based SWD subtypes (SWD-IEs, SWD-Es, and SWD-I) were estimated among hospital shift workers with night shifts (who had ≥ 3 non-day shifts a month). This thesis (Study II) is the first study to report the prevalence estimates of all the three SWD subtypes. Rajaratnam et al. (2011) and Barger et al. (2015) have reported somewhat greater estimates of SWD-IEs prevalence (9%–15%) in their study populations with a male majority than this thesis (Study II, 6%) with a female majority. Although Rajaratnam et al. (2011) did not report the prevalence estimates of the other SWD subtypes, it was possible to approximate the prevalence of SWD-Es (17%) and SWD-I (22%) based on the data provided in their article. These rates were higher than those in this thesis (8% and 4%, respectively). Further, Drake et al. (2004) reported prevalence rates of 1) insomnia and excessive daytime sleepiness (6%), 2) excessive daytime sleepiness without insomnia (16%), and 3) insomnia without excessive daytime sleepiness (10%) among rotating shift workers of the general population. The first rate corresponded to the prevalence of SWD-IEs of this thesis. The latter two prevalence rates were higher than the corresponding SWD prevalence rates of this thesis (Study II). However, instead of SWD subtypes, these percentages among rotating shift workers of the general population represent a general-level insomnia and/or excessive sleepiness, because the symptoms are not uniquely related to shift work, as Drake et al. (2004) state in their article. Thus, comparing these values and the prevalence of the SWD subtypes of this thesis may not be relevant, as the subtype definitions in the studies differ considerably.

6.2 SLEEP AND INSOMNIA IN CONNECTION WITH WORK SHIFTS

It is well known that TST typically decreases in association with early morning shifts and night shifts (Sallinen and Kecklund 2010). Accordingly, short (≤ 6 hours) sleep was also commonly related to night and morning shifts in both the SWD and reference groups of the field study on ground staff of this thesis (Study III). The objectively measured TST in the groups did not significantly differ in relation to any work shift or days off. However, the diary-based TST was shorter before morning shifts in the SWD group than in the reference group. No group differences in TST were found (with any method) after night shifts. Gumenyuk et al. (2014) found that diary-based sleep related to permanent night shifts was shorter among those with SWD than those without SWD. Similarly, Kalmbach et al. (2015) found a comparable difference in a survey study related to weekdays with unspecified shift types. The results of this thesis (Study III) indicate for the first time, to my knowledge, that SWD is associated with a decrease in TST before morning shifts.

Based on the field measures, sleep quality appeared to be poorer in the SWD group than in the reference group (Study III). This was indicated by poorer subjective quality of sleep, lower actigraphy-based sleep efficiency, and longer diary and actigraphy-based sleep latency. Similar differences have been observed in questionnaire-based sleep quality related to swing-shift workers' four-week non-work periods (Waage et al. 2009) and in diary-based sleep efficiency related to permanent night workers' night shifts (Gumenyuk et al. 2014). Interestingly, both study groups in Study III had rather good sleep latency, sleep efficiency, and self-evaluated quality of sleep over the different days. Thus, sleep quality appeared to be rather good in both groups. However, despite this, the measures indicated that the SWD group had a poorer capacity for sleep than the reference group, in connection with morning, evening, and night shifts, and days off.

De-stressing before bedtime forms a part of good sleep hygiene (Porkka-Heiskanen et al. 2013). Karhula et al. (2013) have shown that higher job strain among shift working nurses is associated with difficulties initiating sleep, a symptom of insomnia characteristic of SWD. The SWD group of this thesis (Study III) scored higher points on the bedtime stress scale than the reference group in relation to different shifts and days off. A recent questionnaire study found similar results regarding bedtime stress as part of a general-level sleep hygiene index (Booker et al. 2020a). In addition, Kalmbach et al. (2015) have shown that sleep reactivity, which refers to the sensitivity of an individual's sleep to stress, can predict SWD. Although the ground staff with SWD in this thesis (Study III) were relatively calm and relaxed in association with work shifts, they were calmer and more relaxed on days off. Thus, learning stress management strategies related to shift work days through, for example, sleep hygiene training, might alleviate the symptoms of SWD (Järnefelt et al. 2020) in this group.

6.3 SLEEPINESS AND ALERTNESS IN CONNECTION WITH WORK SHIFTS

The SWD group had more performance lapses in PVT than the reference group at the beginning of night shifts (Study III). In addition, the SWD group's KSS sleepiness reached a high level (> 6) (Åkerstedt et al. 2014) at the end of night shifts, being greater than in the reference group. The median of the greatest KSS sleepiness value was especially high during night shift (8) and morning shift (7.5) days in the SWD group. In fact, based on either the greatest daily KSS or the last five minutes' KSS values, the SWD group appeared to be sleepier than the reference group in connection with all the studied shifts. Days off also showed a similar tendency. In a laboratory study, permanent night workers showed increased sleepiness at night-time in association with SWD (Gumenyuk et al. 2014). This supports the findings of the thesis (Study III), concerning night shifts, although findings of laboratory studies in the context of permanent shift systems cannot be generalised to apply to real-life work with different work shifts as such. To conclude, this thesis (Study III) indicated that in addition to night shifts, SWD-associated sleepiness can also increase in connection with morning and evening shifts.

6.4 RECOVERY FROM SWD

6.4.1 INSOMNIA ON DAYS OFF

SWD was negatively associated with insomnia on days off in the epidemiological study (II) of this thesis. Unlike insomnia in general, SWD-related insomnia stems from work shifts, and should thus improve in the absence of them, which seemed to happen in the SWD group of this thesis (Study II). The improvement implies that the SWD screening instrument of this thesis has the power to differentiate SWD-related insomnia from other insomnia types, as intended. The analyses of SWD subtypes showed that SWD was not significantly associated with insomnia on days off (Study II). Insomnia was not observed in connection with days off in the field study (Study III) either, which is in line with the results of Waage et al. (2009), who found no significant association between SWD and questionnaire-based insomnia during a four-week non-work period. However, the field study (Study III), like Gumenyuk et al. (2015), linked SWD to poorer capacity for sleep, although contrary to the findings of this thesis, Gumenyuk et al. (2015) found that SWD-I associated with a pathological sleep latency on days off among permanent night workers. The findings of this thesis suggest that insomnia rarely disturbs recovery on days off in SWD. However, the findings of Gumenyuk et al. (2015) also reflected the applied criteria for SWD that accepted insomnia on days off as an SWD criterion. In contrast, the criteria used in this thesis only qualified as SWD cases those individuals whose symptoms related to work shifts but did not occur during a holiday.

6.4.2 SLEEPINESS ON DAYS OFF

The field study (III) of this thesis showed only a tendency towards greater KSS sleepiness on days off among the SWD cases than in the reference group of ground staff, whereas the epidemiological study (II) showed an association between SWD (that was not classified into subtypes) and excessive sleepiness on days off among hospital employees. Of the SWD subtypes, only SWD-I was associated with excessive sleepiness on days off (Study II). One should remember that, in addition to SWD-Es and SWD-IEs cases whose SWD is characterised by shift-related excessive sleepiness, many of the SWD-I cases could also have experienced excessive sleepiness during workdays. Nevertheless, excessive sleepiness among SWD-I cases was most likely caused by something other than working hours, because in contrast to the applied SWD definition, it did not improve during a longer recovery period. This can, to some extent, explain why SWD-I appeared to leave a proportion of hospital employees excessively sleepy on days off. In line with this, Waage et al. (2014) showed that a general-level daytime sleepiness predicted SWD among nurses. This thesis adds to this knowledge by showing signs of incomplete recovery on days off particularly related to SWD-I.

6.4.3 SLEEP

An earlier survey study found shorter sleep on weekends among new rotating shift workers with SWD than among those without SWD (Kalmbach et al. 2015). On the contrary, TST on days off did not differ in the study groups in the field study (Study III) of this thesis, nor among the permanent night workers in a sleep diary study by Gumenyuk et al. (2014). However, in Study III, the SWD group reported significantly greater sleep need than the reference group. Longer sleep need may predispose to SWD. Lower sleep quality and greater sleepiness, which were observed in the SWD group of this thesis (Study III), may also elevate estimates of sleep need.

The SWD group (Study III) had greater sleep debt before morning shifts and shorter compensatory sleep on days off than the reference group. It is possible that poorer sleep quality leads to slower recovery from shift work in individuals with SWD, which may then appear as sleep debt. Likewise, better sleep quality and consequently reasonable recovery already during the work period among individuals without SWD can cause shorter sleep debt before morning shifts. Those without SWD may also be able to extend sleep (Rupp et al. 2009; Arnal et al. 2015; Axelsson and Vyazovskiy 2015) on days off to facilitate recovery during the following work period, unlike those with SWD.

The length of SWS appears not to be associated with SWD in this thesis (Study III). Instead, the poorer recovery of the ground staff with SWD is more likely to be linked to less efficient sleep. Nevertheless, the SWD group had less light sleep on days off than the reference group. This supports the idea that recovery may be slower in the SWD group than in reference group, as SWS typically increases during recovery sleep, which can then reduce the length of light sleep (Jay et al. 2007). Therefore, those with SWD could benefit from a longer recovery period.

The epidemiological study (Study II) concentrated on subjective 24-hour sleep length on a general level among hospital shift workers with night shifts but found no association between SWD (which was not classified into subtypes) and sleep length. This finding is supported by survey studies of rotating workers in the general population (Drake et al. 2004; Di Milia et al. 2013). On the other hand, the same survey studies have associated SWD with shorter sleep among permanent night workers (Drake et al. 2004) and in a combined group of dayworkers and rotating workers (Di Milia et al. 2013). Although sleep time is typically reduced in connection with specific shifts in shift work (Sallinen and Kecklund 2010), sleep reduction may not appear in general-level sleep length estimates, as estimation of general-level sleep length can be difficult in shift work, and individuals can compensate for curtailed sleep during free time. This phenomenon may explain the findings of Härmä et al. (2018), who showed that non-day shifts are associated with both difficulties falling asleep and long sleep. In this thesis (Study II), SWD-I was associated with shorter 24-hour sleep among hospital workers with night shifts. When Gumenyuk et al. (2015) studied the insomnia subtypes of SWD among permanent night workers, SWD-IEs in particular was associated with shorter shift-related TST. Nevertheless, the findings of Study II of this thesis imply that it may be difficult for those with SWD-I to get enough sleep to compensate for shift-related sleep deprivation and to overcome excessive sleepiness on days off. This is in line with the findings of the field study of this thesis (Study III), which showed limited compensatory sleep on days off in the SWD group. For example, less flexible sleeping habits that have previously been associated with SWD (Flo et al. 2012), and in this thesis among ground staff (Study III), may make recovery difficult for shift workers.

6.5 METHODOLOGICAL ASPECTS

To find appropriate treatment options (Wright et al. 2013; Järnefelt et al. 2020), it is relevant to make a distinction between the symptoms of insomnia and excessive sleepiness specifically related to shift work schedules (that is SWD) and symptoms caused by other conditions (AASM 2005; Wright et al. 2013; AASM 2014). To classify SWD in this thesis, the shift-related symptoms of the screening questionnaire had to decrease during a two-week holiday. Classifying holiday-related symptoms of insomnia and excessive sleepiness as unrelated to SWD was a strength of this study, as it probably prevented confusing an SWD with other diagnosed or non-diagnosed conditions that included continuing insomnia or sleepiness.

As far as I am aware, the field study (Study III) of this thesis is the first to verify a disturbed sleep-wake pattern among those with SWD using sleep diaries and actigraphy (as stated in ICSD). In addition, Studies I and III are the first to comply with the criterion of reduced TST of ICSD-3. ICSD-3-based SWD was specified if there was an indication of sleep reduction in addition to a primary symptom of SWD. If sleep time was not assessed, SWD corresponded to the ICSD-2 criteria. Thus, the definition of SWD was based on either ICSD-2 or ICSD-3 criteria referring to the coding manual that the applied SWD definition most closely resembled. To my knowledge, this was the first time that both the ICSD-2 and ICSD-3 criteria for SWD have been studied (Study I), or that all the three main subtypes of SWD have been explored in an epidemiological setting (Study II).

The ICSD-2 criteria were used in this thesis for three reasons: 1. To make the comparison between the previous literature and this thesis (Studies I and II) easier. This is because the previous literature has not included the reduction of sleep time as a criterion of SWD (this thesis used it as a criterion of ICSD-3-based SWD). 2. The most recent criteria for SWD, in ICD-11, do not require reduced sleep as a criterion for SWD. 3. To be able to study whether the SWD subtypes are associated with general-level sleep length.

Furthermore, this thesis (Studies II and III) investigated recovery from SWD, which has not been examined a great deal. Another strength of this thesis is that the included epidemiological studies (I and II), as well as the field study (Study III), utilised objective data on working hours to eliminate exposure misclassification. In addition, the same register data were used to specify the number of days linked to SWD symptoms in the epidemiological studies (I and II). Furthermore, this thesis (Study III) was the first to utilise PVT- or EEG-based measures in a real-life setting related to SWD.

Instead of clinical evaluation, which could have confirmed the diagnosis, SWD was defined by a questionnaire. This may be considered a limitation. However, Study III utilised field measurements to verify the condition. Using a questionnaire to define an SWD is typical in SWD research, as SWD is not a widely recognised disorder in healthcare. In addition, SWD lacks an unambiguous operational definition, which is why multiple instruments have been used to define it in the literature.

Based on the ICSD, SWD-related sleep or wake disturbance should not result from another primary condition. However, these conditions can also occur concurrently with SWD (Kerkhof 2018; Waage et al. 2018) or even arise from SWD (Kalmbach et al. 2015). The epidemiological part of this thesis (Studies I and II) included hospital employees suffering depression, sleep apnoea, and RLS, which may have influenced the identification of SWD. However, in Study I, when the individuals with these conditions were excluded from the sensitivity study, the prevalence estimates of SWD changed very slightly (maximum 0.4%). This is in line with the findings of Flo et al. (2012).

In addition, in Study II, these conditions were included in the adjusted analyses. Furthermore, in the field study (III), depression, untreated sleep apnoea, and RLS were exclusion criteria.

The epidemiological studies (I and II) of this thesis included all shift workers. However, to make the interpretation of the results simpler, the field study (III) excluded shift workers with 'mild symptoms' that could not be clearly associated with SWD or lack of SWD. Although a similar approach has been used before (Axelsson et al. 2004; Karhula et al. 2013), it is important to understand that this added to the contrast between the SWD and reference groups in Study III. On the other hand, the inclusion of 'milder SWD cases' could have blurred the comparison between the study groups because it was not clear whether or not the 'milder SWD cases' truly had an SWD. Based on recent literature, a significant proportion of those who screened positive for SWD seem to lose their SWD status by the second screening (Waage et al. 2014; Chen et al. 2020), which was also the case in this study (III). Accordingly, only those whose SWD or reference category remained the same from recruitment to the start of the field measurement period were included in the study, although this reduced the number of participants.

The SWD group was younger than the reference group in the field study (III) of this thesis. The younger age of the SWD group was possibly due to the healthy worker effect (Knutsson and Åkerstedt 1992), as individuals with SWD are probably more likely to leave shift work than those without SWD. The difference in age may have reduced some group differences, as younger age has been shown to associate with longer and better sleep (Ohayon et al. 2004; Costa and Sartori 2007; Boulos et al. 2019), a lower need for recovery (Kiss et al. 2008), and shift work tolerance (Saksvik et al. 2011). Therefore, whenever possible, the analyses were adjusted for age, and alternatively for chronotype.

Late chronotype may cause short sleep before morning shifts, while early chronotype may shorten sleep after night shifts (Juda et al. 2013). In Study III, the proportion of late chronotypes was greater, although not significantly greater, in the SWD group than in the reference group. Although some studies have associated later chronotype with SWD (Asaoka et al. 2013; Waage et al. 2014; Booker et al. 2020a), this does not appear to be the case for all populations (Waage et al. 2009; Taniyama et al. 2015; Chen et al. 2020). Further, the analyses of Study III were not adjusted for potential confounders other than age or chronotype, which can be considered a limitation. Another limitation is that the tests related to non-normally distributed variables could not be adjusted due to the limited sample size of the field study (III).

Although work shifts starting at 06:00–07:00 hours may induce SWD symptoms, they were not classified as non-day shifts in the epidemiological studies (I and II) of this thesis. As a result, some individuals with, for instance, late chronotype, may have been misclassified as non-SWD cases. If the survey had included habitual bed and rise times, the number of shifts that induce the

SWD symptoms could have been evaluated more accurately on an individual level, which may have improved the identification of SWD.

The SWD group of the field study (III) of this thesis exercised more often and consumed less caffeinated drinks than the reference group. Exercise can modify circadian rhythm and improve sleep (Schroeder and Colwell 2013). Thus, those with SWD may have exercised to improve their sleep. However, poorly scheduled exercise can disturb sleep, and could have impaired the SWD group's sleep and alertness in the field study (III) of this thesis. Moreover, caffeine is a stimulant that promotes wakefulness and can thus disrupt sleep (Wright et al. 2013). It has been shown that those whose sleep is impaired as a result of situational stressors (for instance shift work) may also be vulnerable to the sleep-disturbing consequences of caffeine (Bonnet and Arand 2003). These individuals may avoid consuming caffeine before bedtime, which may explain the lower caffeine consumption in the SWD group than in the reference group in this thesis (Study III).

As sufficient recovery from shift work supports health (Merkus et al. 2015), and shift work has been especially associated with fatigue on weekly days off (Härmä et al. 2018; Härmä et al. 2019), fatigue on weekly days off was chosen as an indicator of seriousness of SWD (or minimum occurrence of SWD symptoms) in the epidemiological study (I) of this thesis. In addition to working hours, fatigue can be caused by several other factors, such as work-life balance or the work environment (Smith-Miller et al. 2014). However, a recent study (using the same cohort of hospital employees as this thesis), which controlled for individual characteristics, found that changes in non-day shifts were associated with corresponding changes in fatigue on weekly days off (Härmä et al., 2018). Furthermore, fatigue consists of physical and mental elements, including tiredness, whereas sleepiness relates to sleep propensity (Mullins et al. 2014). However, some individuals may incorporate sleepiness in their fatigue estimation. A limitation of this thesis is that it could not evaluate what exactly caused fatigue, and further, what elements the fatigue estimate included.

This thesis includes subjective single-item measures, which is a limitation. Although register data (Haapanen et al. 1997) and validated questionnaires (Horne and Östberg 1976; Wennman et al. 2015) would be more optimal, single-item scales of, for example, disorders (Haapanen et al. 1997) and chronotype (Wennman et al. 2015) have shown to be usable in epidemiological settings. In the epidemiological study (II) of this thesis, sleep length was self-reported using a single question, which is common in large scale studies (Lauderdale et al. 2008; Girschik et al. 2012). The hospital employees chose one estimate to represent their usual 24-hour sleep length from a scale with 30-minute intervals. This may have been problematic as shift workers' sleep length can vary in relation to different shift types and days off (Girschik et al. 2012). In addition, not all the participants necessarily included daytime naps in their sleep length estimate. Hence, individuals may have interpreted the question in different ways, which adds variation and inaccuracy regarding the sleep length variable. The sleep length estimate could have improved if it had been based on bedtimes and wake-up times in connection with different shift types and days off (St-Onge et al. 2019). Further, insomnia and excessive sleepiness on weekly days off and SWD were evaluated using one set of questions in the epidemiological study (II). As the questionnaire included separate items for weekly days off and for a longer recovery period, the participants most likely did not confuse the length of the two. Sleep need was evaluated subjectively in the field study (III) of this thesis. In a real-life field study, objective evaluation of sleep need may not be possible if complete recovery lasts longer than the recovery periods of everyday life. In addition, although the amount of real life's habitual sleep has been used to estimate sleep need, the actual sleep need may be greater than habitual sleep length (Klerman and Dijk 2005; Kitamura et al. 2016).

The study design of this thesis was cross-sectional, which prevents causal conclusions. In addition, due to the limited number of participants, statistical power was reduced in analyses of hospital employees without night shifts when higher inclusion cut-offs were used (Study I), in analyses of hospital employees categorised into SWD subtypes (Study II), and in analyses of ground staff members (Study III). However, the statistical power was adequate to detect significant differences between the SWD and reference groups in the field study (III). In future research, larger samples could be used to verify the findings of this thesis. Finally, generalisation of the results to shift systems that were not studied in this thesis, i.e., permanent night work, or to other vocational branches should be made with caution.

7 CONCLUSIONS AND FUTURE PERSPECTIVES

This thesis adds to the knowledge on the association between SWD criteria and shift arrangements and the prevalence rate of SWD. In addition, this is the first time that the manifestation of SWD has been observed in association with real-life morning, evening, and night shifts. Furthermore, recovery from the symptoms of SWD was investigated in association with weekly days off in both epidemiological and real-life settings. In line with the major coding manuals, the SWD screening method of this thesis accepted only the symptoms that specifically related to shift work as an indication of SWD.

To conclude, the ICSD-3 criteria produced lower prevalence estimates of SWD than the ISCD-2 criteria in the epidemiological study among hospital employees. Thus, rather than the latest ICSD criteria, to prevent confusion, the studies on SWD should refer to the ICSD criteria that best resembles the applied definition of SWD. In addition, many individuals who, according to the survey, screened as positive for SWD appeared to have only a few days per month with SWD symptoms. This does not correspond to the ICSD criteria. The preliminary results of this thesis indicate that individuals with night shifts who have less than three days per month with insomnia or excessive sleepiness may not be eligible SWD candidates. When the cut-offs for SWD diagnosis and shift work frequency were set at ≥ 3 symptoms and shifts, respectively, per month, the prevalence estimate of ICSD-3-based SWD varied from 3% to 6%, whereas that of ICSD-2 varied from 9% to 18% among the hospital employees. Future studies on SWD should validate the minimum recurrence of SWD symptoms to minimise false positive SWD cases and define the cut-off of non-day shifts to match the concept of shift work.

In the field study (III) of this thesis, the quality of sleep and relaxation at bedtime were poorer overall in the SWD than in the reference group. In addition, the ground staff members with SWD had shorter subjective sleep and greater sleep debt than the reference group before morning shifts, which has not been shown before. In fact, earlier SWD research has not focussed on morning shifts, although morning shifts are known to interfere with sleep and alertness (Åkerstedt 2003). In addition to night shifts, the SWD group was also sleepier than the reference group in connection with morning and evening shifts. The epidemiological study (I) indicated that the timing of non-day shifts does not considerably affect the estimates of SWD prevalence if the SWD symptoms occur at least five times a month. Thus, both the field and epidemiological studies indicate that types of shifts other than night shifts can also cause SWD symptoms. Therefore, these should be considered in future research on SWD.

The field study (III) of this thesis is the first to indicate less compensatory sleep on days off among shift workers with SWD than among those without

SWD. In line with this, the epidemiological study (II) of this thesis associated SWD with excessive sleepiness on days off, indicating poorer recovery on days off among shift workers with SWD than among those without SWD. However, poorer recovery appeared not to be associated with insomnia on days off. Poorer recovery from excessive sleepiness was especially apparent among hospital employees whose SWD was characterised by insomnia only (SWD-I). SWD-I also associated with shorter subjective 24-hour sleep length. Thus, sleep on days off may not be adequate to compensate for the insufficient sleep related to shift work among hospital employees with SWD-I and overcome excessive sleepiness.

The pattern of suboptimal sleep and alertness in connection with shifts and short compensatory sleep on days off, together with poorer flexibility of sleeping habits and less bedtime relaxation described in the field study (III), may unfavourably affect shift workers. This may appear as, for example, excessive sleepiness on days off, which was indicated among hospital employees with SWD in the epidemiological study (II) of this thesis. Compensatory responses are beneficial for shift workers, and both the real-life field observation and epidemiological findings concerning SWD pointed towards poorer compensatory responses during free time in SWD. SWD appears to be associated with less efficient recovery. Future studies should investigate whether individuals with SWD would benefit from individualised shift scheduling or extending recovery periods on rosters. For example, individuals with SWD-I might benefit more from extension of recovery periods than those with other SWD subtypes. Investigating this may enable more efficient allocation of interventions at workplaces.

This thesis also revealed a trait-like feature of SWD: poorer sleep quality, which in turn can make recovery slower. If working time features that give rise to SWD cannot be avoided, the health, work ability, and safety of shift workers may be managed by promoting circadian adaptation, sleep, and alert wakefulness (Wright et al. 2013). If the symptoms of SWD cannot be alleviated by individual, organisational, or medical means, an individual may be forced to change workplaces or professions. Future intervention studies could investigate whether educating individuals in the demands of shift working hours, with respect to their own abilities, before they enter vocational education, could prevent vulnerable individuals entering professions that involve shift work.

Although SWD is common among shift workers, it is a rarely used diagnosis. One reason for this is the lack of established instruments in healthcare for identifying an SWD. An SWD can be confused with other conditions that show symptoms of insomnia or excessive sleepiness, which can delay finding the right cure. Therefore, SWD should be considered when treating shift workers with symptoms of insomnia or excessive sleepiness. The SWD screening tool that was applied in this thesis could be utilised in healthcare, as it distinguished an SWD from some other conditions with similar symptoms. In Finland, the majority of the employed workforce is covered by occupational health services which makes these services a natural environment to reach and identify individuals with SWD. Thus, to find an effective cure for patients, as well as to make the most of the coding manuals of disorders, occupational health services should be familiarised with SWD diagnosis. This study also suggests a minimum cut-off for SWD symptoms, which could be applied in occupational health services together with the SWD screening instrument, though further research is needed to validate the cut-off. Based on the findings of this thesis, in addition to night shifts, symptoms that occur in association with morning and evening shifts are also relevant for diagnosing an SWD.

ERRATA

PUBLICATION III

On page 528 in the ‘Subjective sleepiness and objective alertness’ section, the words ‘means’ and ‘mean’ should be ‘medians’ and ‘median’, respectively.

On page 531 in the second paragraph of the ‘Limitations’ section, ‘after a shift work washout period’ should be ‘with respect to a shift work washout period’.

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